Medical TIMES

THE JOURNAL OF GENERAL PRACTICE

VOL. 83 SEPTEMBER 1955 NO. 9

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it's easy. Mothers find they blend
readily with the formula, milk,
or juice, and youngsters often
like them 'straight'. Either way,
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full potency.
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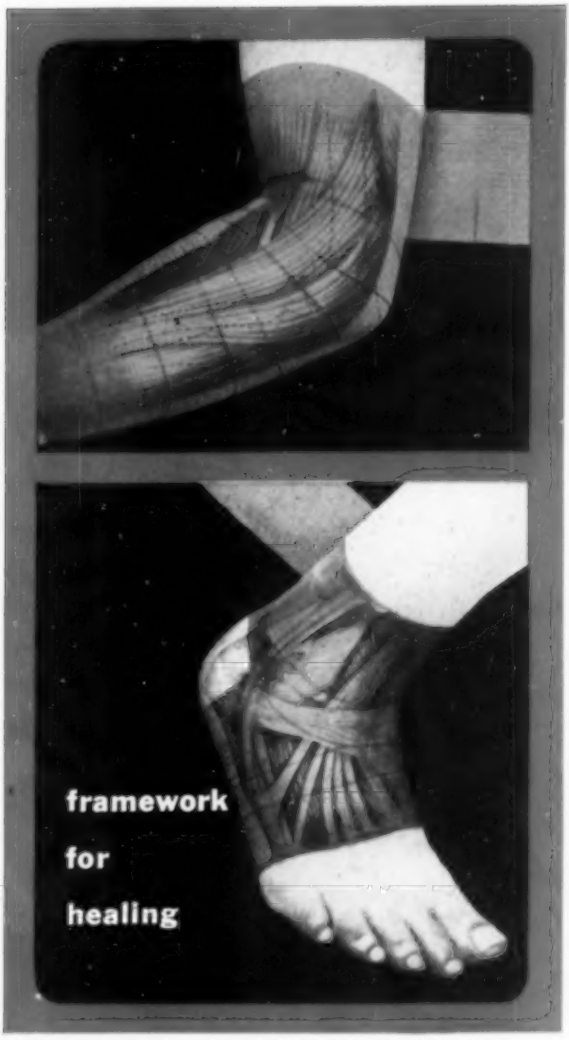

ACE® RUBBER-ELASTIC BANDAGE

elasticity for compression

body for support

B-D BECTON, DICKINSON AND COMPANY, RUTHERFORD, N. J.

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Tourist Souvenir . . .

Memorable beauty, pastoral charm, vacationer's diarrhea. . . .
To combat susceptible *infectious* forms, STREPTOMAGMA exerts potent antibacterial, adsorptive, and protective actions. Soothes the bowel, encourages normal stool development.
For common noninfectious diarrheas, prescribe KALPEC®—pectin with kaolin in alumina gel.

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CONTENTS

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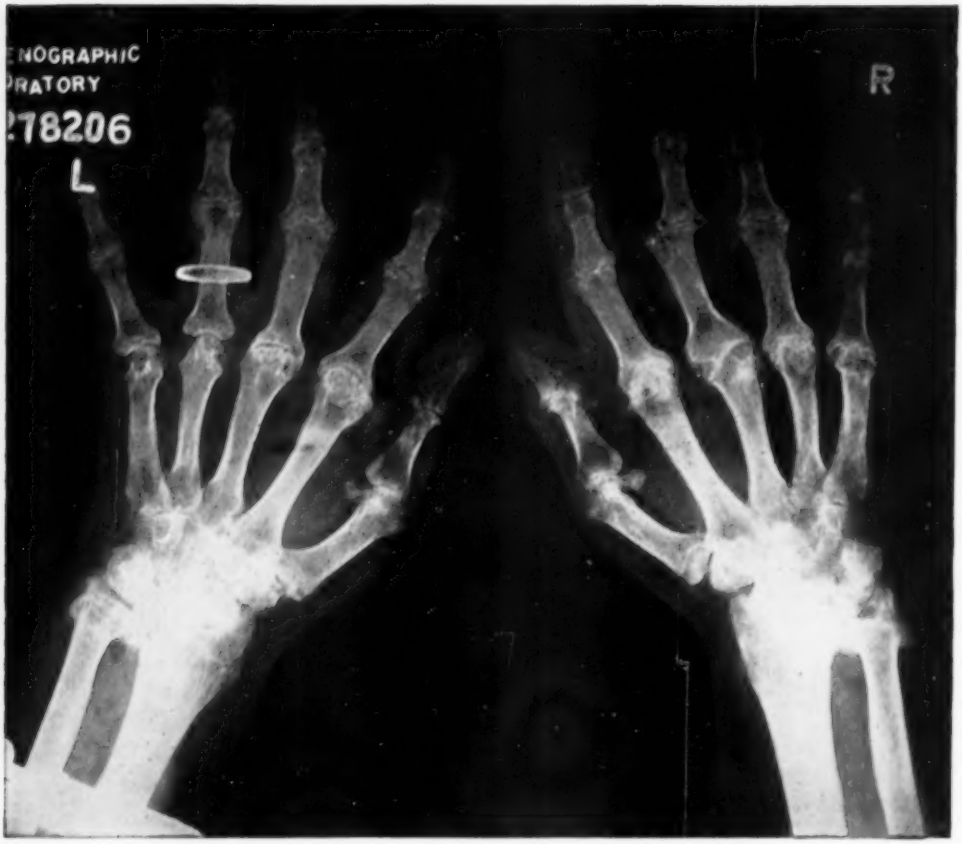


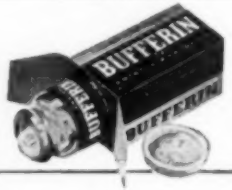
BUFFERIN®—*THE BETTER-TOLERATED SALICYLATE FOR RHEUMATOID ARTHRITIS*

Gastric upsets from aspirin are 3 to 9 times as frequent among arthritics as they are among the general population.[1] However, BUFFERIN is well tolerated by arthritics. At the Robert Breck Brigham Hospital of Boston 70 per cent of arthritics with a proved intolerance to aspirin could take BUFFERIN without gastric distress.[2]

Although patients often use sodium bicarbonate with aspirin to alleviate gastric symptoms, clinicians know that this causes a lowering of the salicylate level of the blood serum.[3] Moreover, this practice may cause retention of the sodium ion.[4] Pre-existing symptoms of cardiorenal disease have been aggravated.[5]

IN ARTHRITIS—WHEN LARGE AND PROLONGED SALICYLATE DOSAGE IS INDICATED, GIVE BETTER-TOLERATED BUFFERIN.

Each BUFFERIN tablet combines 5 gr. acetylsalicylic acid with magnesium carbonate and aluminum glycinate. BUFFERIN is available in bottles of 12, 36, 60 and 100 tablets.



References: 1. Fremont-Smith, F.: J.A.M.A. 158:386, 1955. 2. J.A.M.A. 161:124, 1949. 3. M. Times 81:41, 1953.

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DOES NOT UPSET THE STOMACH

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19 West 50 Street, New York 20, N. Y.

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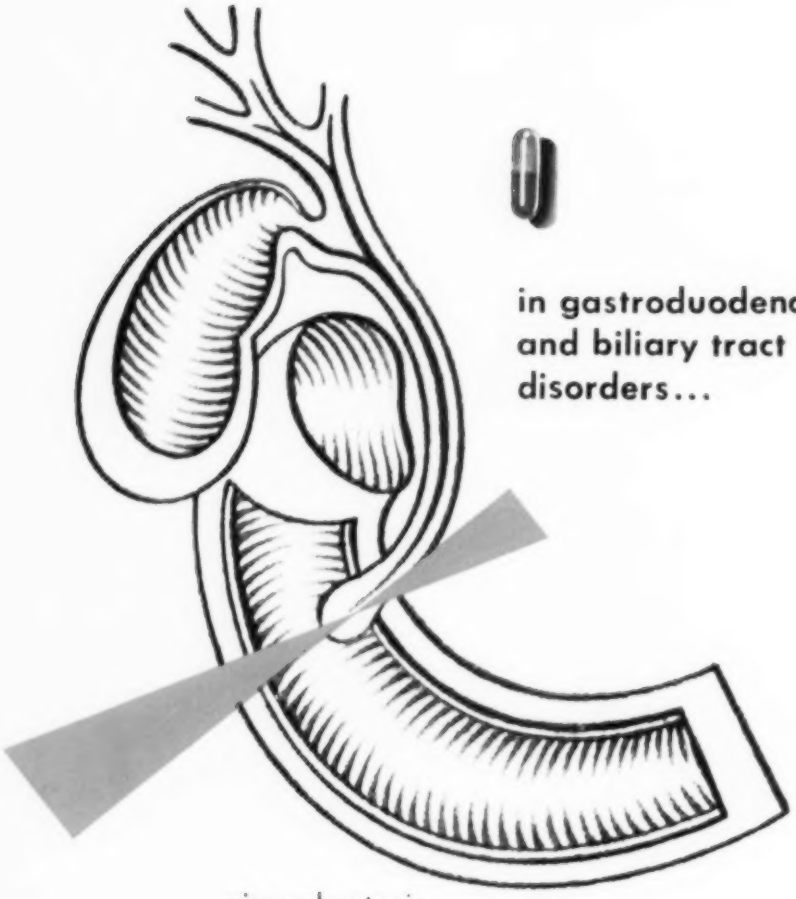


in gastroduodenal and biliary tract disorders...

visceral eutonic

DACTIL

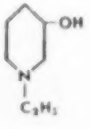
PLAIN AND WITH PHENOBARBITAL

relieves **pain** ⇄ **spasm** *usually in 10 minutes*

prompt action at the site of visceral pain gives unusually rapid relief

prolonged control of spasm gives relief up to four hours

no interference with digestive secretions, normal tonus or motility



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EFFECTIVE

Over 96 per cent live delivery in 1200 patients . . . *including 540 habitual aborters.*[1]

SAFE

No side effects in pregnant patients . . . *in either low or massive dosage.*[2]

COMPREHENSIVE

A Formulation Proved By Extensive Clinical Experience,[1, 2, 3, 4]

— Each **desplex** tablet contains 25 mg. of rapid-acting *ultra*-micronized diethylstilbestrol U.S.P., with protective and effectuating amounts of vitamin B complex and vitamin C.

— For further information and a generous trial supply of **desplex**, write to:

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Grant Chemical Co., Inc.

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REFERENCES

1. Peña, E. F.: Med. Times 82:921, 1954; Am. J. Surg. 87:95, 1954
2. Karnaky, K. J.: South. M. J.: 45:1166, 1952
3. Gitman, L. and Koplowitz, A.: N. Y. St. J. Med. 50:2823, 1950
4. Ross, J. W.: J. Nat. M. Assoc. 43:20, 1951; 45:223, 1953

Medical TIMES

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WELL TOLERATED BROAD SPECTRUM ANTIBACTERIAL THERAPY PLUS ANTIFUNGAL PROPHYLAXIS

BROAD SPECTRUM ANTIBIOTIC THERAPY, EFFECTIVE IN MANY COMMON INFECTIONS

Because it contains Steclin (Squibb Tetracycline), MYSTECLIN is an effective therapeutic agent for most bacterial infections. When caused by tetracycline-susceptible organisms, the following infections are a few of those which can be expected to respond to MYSTECLIN therapy:

bronchitis	gonorrhea	osteomyelitis	pyelonephritis
colitis	lymphadenitis	otitis media	sinusitis
furunculosis	meningitis	pneumonia	tonsillitis

MYSTECLIN is also indicated in certain viral infections and in amebic dysentery.

BROAD SPECTRUM ANTIBIOTIC THERAPY, WITH A MINIMUM OF SIDE EFFECTS

In clinical use, Steclin has produced an extremely low incidence of the gastrointestinal distress sometimes observed with other broad spectrum antibiotics. Mycostatin (Squibb Nystatin), as contained in MYSTECLIN, is also a particularly well tolerated antibiotic and has produced no allergic reactions, even after prolonged administration.

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Because it contains Mycostatin, the first safe antifungal antibiotic, MYSTECLIN effectively prevents the overgrowth of Candida albicans (monilia) frequently associated with the administration of ordinary broad spectrum antibiotics. This overgrowth may sometimes cause gastrointestinal distress, anal pruritus, vaginitis, and thrush; on occasion, it may have serious and even fatal consequences.

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Each MYSTECLIN capsule contains 250 mg. Steclin Hydrochloride and 250,000 units Mycostatin.

Minimum adult dose: 1 capsule q.i.d.

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potent anti-diarrhea agent now available in the U.S.A.

Entero-Vioform, a powerful agent for use in simple infectious diarrhea and amebic dysentery, is now available for the first time in the United States. This well-tolerated, virtually nontoxic anti-diarrhea agent is especially useful for travelers, who are particularly vulnerable to diarrhea.

Entero-Vioform is available in tablets (also known as Vioform® tablets), each containing 250 mg. iodochlorhydroxyquin U.S.P.

VIOFORM® (iodochlorhydroxyquin U.S.P. CIBA)

CIBA
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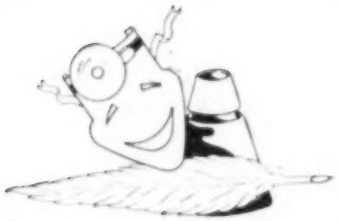


Off the Record . . .

True Stories From Our Readers

Each incident described has been contributed by one of our readers. Contributions describing actual and unusual happenings in your practice are welcome. For obvious reasons only your initials will be published. An imported German apothecary jar will be sent in appreciation for each accepted contribution.

Quiet Conditions

Mr. Gahn was on a salt-poor diet because of a heart condition. I decided to put him on Walker Gordon's Lo Sodium Raw Milk.

"Why do I need a prescription to order milk?" he asked. I replied that it was raw milk, not pasteurized, but that it was safer than the pasteurized milk because of the care, cleanliness and expert supervision in the production of the raw milk by the Medical Society. I also explained an Rx was required by city law.

"Yes, I understand why the milk is so good," Mr. Gahn said, "it is prepared under cemetery conditions."

M.L.S., M.D.
New York, New York

An Afterthought!

As a young 1st Lt., I was proud of my new assignment as Chief of EENT in a small air force hospital. We had a nice building, but equipment was meagre. Certainly no such thing as a blood transfusion was feasible. My first duty as EENT chief was to deliver the 4th child of a full colonel's wife. I held up to the ordeal rather well until the good woman said rather nonchalantly, "By the way doctor, it took 4 pints of blood to get me through the last one."

She did well but I became old on the spot.

W.B.N., M.D.
Longview, Texas

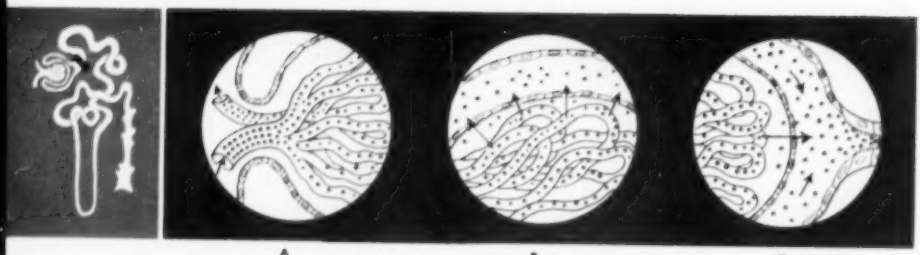
The case of the Missing . . .

After leaving my office, a patient called my secretary and asked her if she would look in the dressing room in order to determine whether or not the patient had left her panties there.

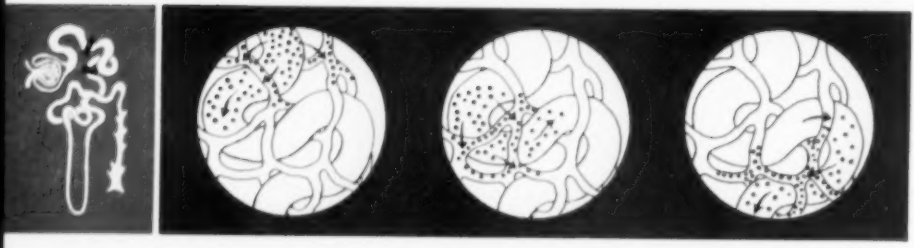
After a frantic search involving my secretary, technician, janitor, my wife (who happened to be in the office at the time), her mother and several patients who joined in the search, my secretary finally had to report in dismay that they could not be found.

As soon as she was given this dis-

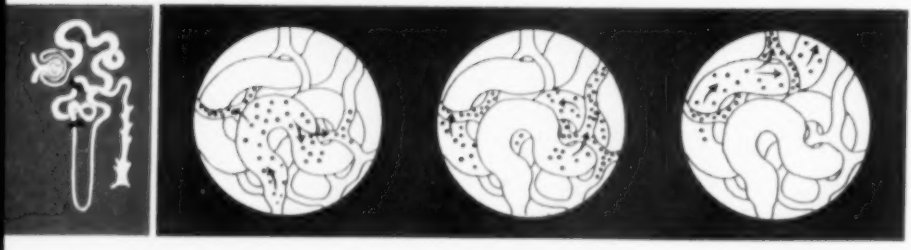
Continued on page 18a



Sodium is one of several ions and substances excreted in the glomerular filtrate; (a) afferent and efferent arterioles, (b) passage of ions into Bowman's capsule, (c) sodium ions entering the proximal tubule.



In the proximal convolated tubule reabsorption of water, electrolytes and other substances begins as the glomerular filtrate traverses the tubule. Among the substances reabsorbed are sodium ions.

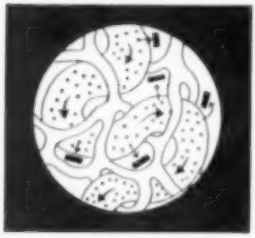


Additional reabsorption into the blood stream takes place in the distal convoluted tubule. In the normal kidney reabsorption is controlled by a selective process according to body requirements.

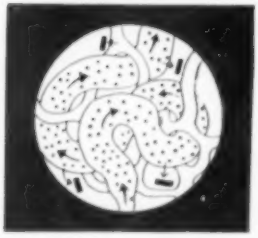
MICTINE*—THE NEW ORAL DIURETIC

Searle MICTINE Provides Effective Oral, Non-Mercurial Diuresis

The result of many years of research, Mictine, brand of aminometramide, supplies a long-felt need for an improved oral diuretic. Mictine, 1-allyl-3-ethyl-6-aminotetrahydropyrimidinedione, is not a mercurial, xanthine or sulfonamide.



Mictine is believed to act by the selective inhibition of the reabsorption of sodium ions; the exact mechanism of this action is unknown. On administration of Mictine chloride ions in equimolar proportions to sodium ions appear in the urine.



Thus, the resulting diuresis is characterized by increased but equimolar quantities of sodium and chloride ions and, of course, water.

SEARLE

Effectiveness: Every method for measuring the diuretic effect in man now available, including precise human bioassay studies, without exception demonstrated that Mictine is an effective oral diuretic, and these studies show that approximately 70 per cent of *unselected* edematous patients treated with Mictine by mouth respond with a satisfactory diuresis.

Well-Tolerated: There are no known contraindications to Mictine, even in the presence of hepatic or renal damage, and there is no risk of acidosis. On high dosage, Mictine causes some side effects in some patients but on three tablets daily these side effects (anorexia and nausea, rarely vomiting, diarrhea or headache) are minimal or absent.

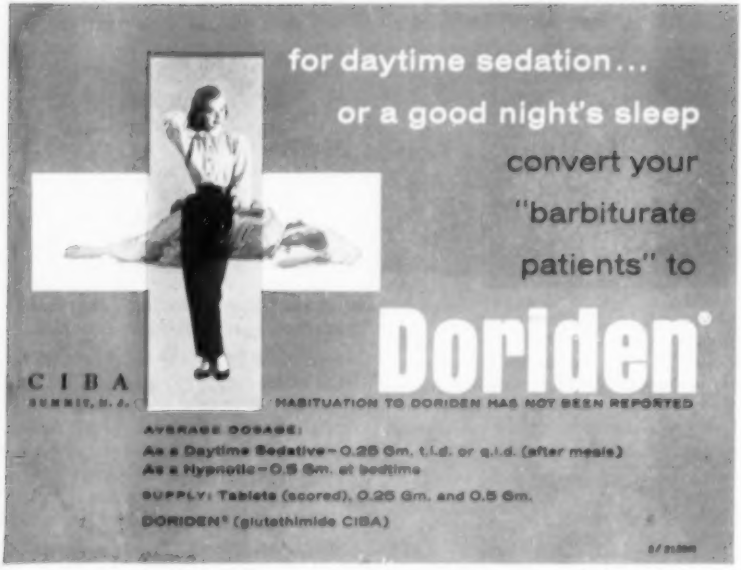
Indications: Mictine is useful primarily in the maintenance of an edema-free state and in the *initial and continuing* control of patients in mild congestive failure. Mictine may be used also for *initial and continuing* diuresis in *more severe* congestive states, particularly when mercurial diuretics are contraindicated.

Administration: The usual dosage for the average patient is one to four tablets daily with meals, in divided doses on an interrupted schedule. An interrupted dosage schedule may be accomplished by giving the drug on alternate days or for three consecutive days and then omitting it for four days.

For severe congestive states the dosage is four to six tablets daily with meals, in divided doses on interrupted schedules similar to those already mentioned.

Supplied: Uncoated tablets of 200 mg.

*Trademark of G. D. Searle & Co.


for daytime sedation...
or a good night's sleep
convert your
"barbiturate
patients" to
Doriden®
CIBA
SUMMIT, N. J.
HABITUATION TO DORIDEN HAS NOT BEEN REPORTED
AVERAGE DOSAGE:
As a Daytime Sedative—0.25 Gm. t.i.d. or q.i.d. (after meals)
As a Hypnotic—0.5 Gm. at bedtime
SUPPLY: Tablets (scored), 0.25 Gm. and 0.5 Gm.
DORIDEN® (glutethimide CIBA)

—Concluded from page 15a

heartening news, the patient apologized and stated, "Oh Mrs. C., I am so sorry that I put you to all this trouble. When you left the phone to look for my panties, I remembered that I had left them at the dentist."

With this, my secretary quickly replied, "Of course, I remember you told me you were going to have some cavities filled."

J.W.E., M.D.
Baltimore, Maryland

Please, Doc!

Mr. Anderson was suffering from a bout of prolonged diarrhea. He came to my office one day, dressed in his Sunday best.

"What do you say, Doctor? When are you going to cure me? Have mercy on me. After all, I haven't had a formal movement for over a year."

M.L.S., M.D.
New York, New York

Just in Time

One afternoon, a woman rushed into my office saying, "My 16 year old daughter is having a miscarriage and I would like you to have a look at her." The young girl was obviously suffering considerably. The nurse placed her on the table and upon examination, I found the young lady completely dilated with a head presenting—Yes, we delivered an eight pound healthy boy. It was a full term miscarriage.

P. J., M.D.
Sapulpa, Oklahoma

Pharmacist Needed

A young woman came to my office with an abscess. After opening and draining it, I advised her to go home and use some hot epsom salts packs, using a cup of epsom salts to a gallon of water and using her hot water bottle or heating pad to keep the packs hot longer.

A few days later she returned with very little improvement. I asked if she had used the hot packs as I suggested. She said yes and went on to explain that she had very carefully measured the epsom salts and put it in her hot water bottle.

S. J. B., M.D.
Tulsa, Oklahoma

Check Up

A squatty obese female with a very poor credit rating came to my office one busy afternoon with her sick child. After prescribing for the child she suggested I give her a check up. I requested that she wait and come alone some day. I had hoped she would abandon the idea.

Later in the day, the child phoned that her mother was ill. I advised aspirin and heat to the abdomen. A few hours later a neighbor lady phoned to advise me that the baby was about here. I hurried and met the patient at the hospital in time to help in the delivery of a full term normal child.

I. R. M., M.D.
Atchison, Kan.

Today's foremost antibiotic!

ACHROMY

—true broad-spectrum activity

—rapid diffusion and penetration

—prompt control of infection

—negligible side effects

—effective against Gram-positive and Gram-negative bacteria, rickettsia, spirochetes, certain viruses and protozoa

—produced under rigid quality control in Lederle's *own* laboratories

CIN

TETRACYCLINE *Lederle*

DOSAGE FORMS FOR EVERY NEED . . . A CHOICE OF POTENCIES!

New!

ACHROMYCIN Sf

ACHROMYCIN WITH STRESS FORMULA VITAMINS

dry filled sealed capsules—a Lederle exclusive! No oil, no paste, tamper-proof. More rapidly and completely absorbed. Stress vitamin formula as suggested by the National Research Council. Prescribe ACHROMYCIN SF for prompt control of infection and rapid patient recovery, particularly in prolonged illness. *Capsules of 250 mg.*

Also available: ACHROMYCIN SF Oral Suspension: 125 mg. per teaspoonful (5 cc.), 2 oz. bottle.

Lederle

LEDERLE LABORATORIES DIVISION *American Cyanamid Company* Pearl River, New York

itching, scaling, burning

SELSUN acts quickly to relieve seborrheic dermatitis of the scalp. Itching and burning symptoms disappear with just two or three applications—scaling is controlled with just six or eight applications. And SELSUN is effective in 81 to 87 per cent of all seborrheic dermatitis cases, 92 to 95 per cent of dandruff cases. Easy to use, SELSUN is applied and rinsed out while washing the hair. Takes little time, no messy ointments or involved procedures. Prescribe the 4-fluidounce bottle for all your seborrheic dermatitis patients. Complete directions are on label.

Abbott

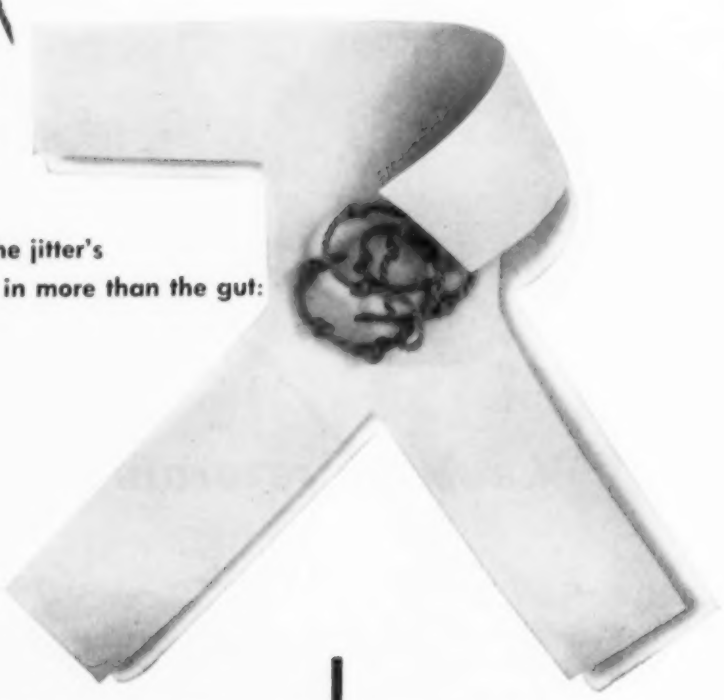
®SELSUN *Sulfide Suspension / Selenium Sulfide, Abbott*

keep returning?

your patient needs

SELSUN®

When the jitter's
in more than the gut:



Serpedon

the tension-easing antispasmodic

Serpedon* helps you treat the jittery patient with the jittery gut, not just his spasm, which is most likely a symptom of his real trouble: anxiety and tension. Serpedon is 0.1 mg. reserpine, plus three alkaloids of belladonna, equivalent to 7 minims of the tincture. Serpedon rescues the patient from his symptom-producing anxiety and tension with reserpine . . . tranquilizes him, doesn't dull him. Serpedon stops spasm . . . stops it quickly, gives reserpine time to exert its full, tension-easing effect.
Recommended dose is one tablet t.i.d. Supplied in bottles of 100 scored tablets.

Walker Laboratories, Inc., Mount Vernon, New York

*trademark

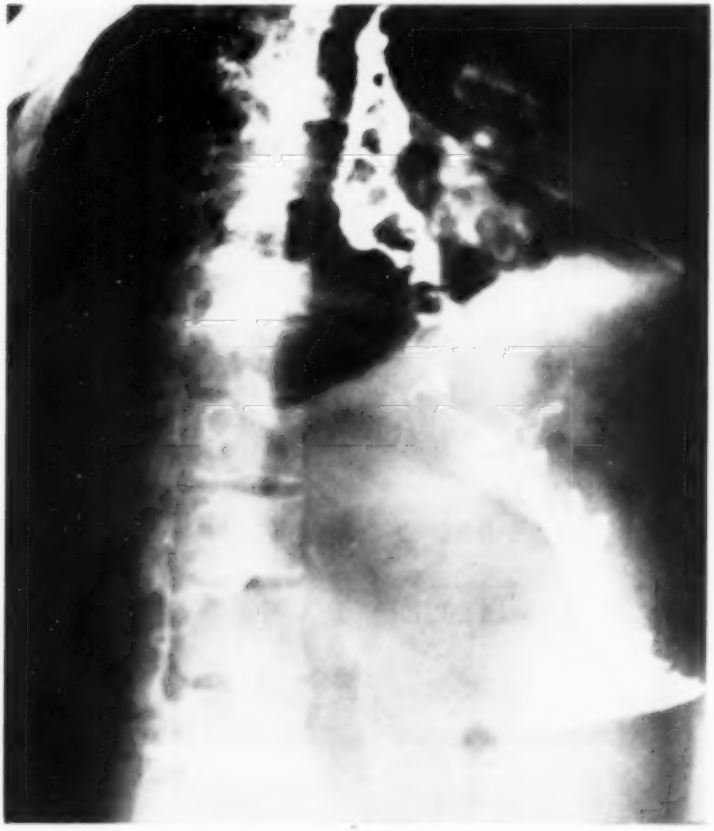
Diagnosis, Please!

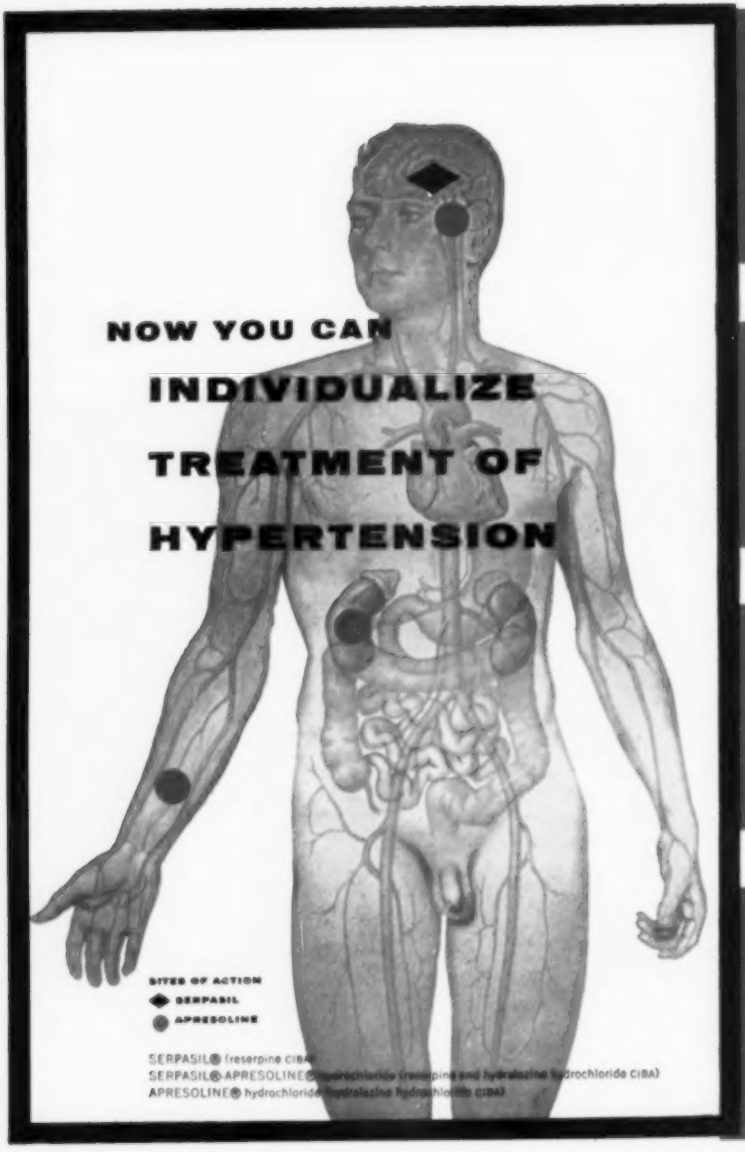
Edited by Maxwell H. Poppel, M.D., F.A.C.R., Professor of Radiology,
New York University College of Medicine and Director of Radiology, Bellevue Hospital Center

WHICH IS *YOUR* DIAGNOSIS?

1. Carcinoma of esophagus
2. Food in esophagus
3. Clots in esophagus
4. Polypi
5. Esophageal Varices

(ANSWER ON PAGE 106a)

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INDIVIDUALIZE
TREATMENT OF
HYPERTENSION
SITES OF ACTION
SERPASIL
APRESOLINE
SERPASIL® (reserpine CIBA)
APRESOLINE® hydrochloride (hydralazine hydrochloride CIBA)

For initial therapy—in all cases:

SERPASIL, a pure crystalline alkaloid of rauwolfia root—particularly effective in the neurogenic forms of hypertension. *Acts centrally*—tranquilizes, moderately lowers blood pressure, slows heart rate.

Serpasil®

When combination therapy is indicated:

SERPASIL-APRESOLINE, a combination product offering convenience and economy in the more complicated cases involving both neurogenic and humoral factors.

Serpasil®-Apresoline®

In more refractory cases requiring further individualization of dosage:

APRESOLINE *acts centrally and peripherally* for a marked antihypertensive effect. Increases renal plasma flow—produces vasodilatation—inhibits pressor substances.

Apresoline®

Serpasil	Tablets, 0.1 mg., 0.25 mg. and 1.0 mg. Parenteral Solution (for neuropsychiatric use only), 2.5 mg. per ml., in 2-ml. ampuls. Elixir, 0.2 mg. per 4-ml. teaspoonful.
Serpasil-Apresoline	Tablets, each containing 0.1 mg. of Serpasil and 25 mg. of Apresoline. Tablets, each containing 0.2 mg. of Serpasil and 50 mg. of Apresoline.
Apresoline	Tablets, 10 mg., 25 mg., 50 mg. and 100 mg. Ampuls, 1 ml., 20 mg. per ml.

CIBA
SUMMIT, N. J.

to help you relieve **muscle spasm** *and* **pain** *safely in* **more rheumatic** *patients*

mephosal®

Relaxant mephenesin, "solubilized"* and made more predictable, with analgesic sodium salicylate. With MEPHOSAL your patients get . . . .

1. Surer relief from muscle pain and spasm; **2.** Greater comfort-in-motion, the ability to move around, work, live more normally, and **3.** Less likelihood of crippling disablement or postural deformity, since muscle rigidity and atrophy are avoided or minimized.

MEPHOSAL is safe, risk-free and worry-free. Will not affect blood pressure, produce or influence diabetes, or produce steroid effects.

Try **MEPHOSAL** first in **LOW BACK PAIN, PAINFUL SHOULDER, STIFF NECK, NIGHT CRAMPS,** or wherever you must relieve muscle spasm and pain promptly.

For Best Results start with full dosage: at least 2 Capsules or 3 Tablets, or 1 to 2 teaspoonfuls Elixir, 3 or 4 times a day, with milk or after meals. After 2 days reduce to 1 capsule, 2 tablets, or 1 teaspoonful elixir, as necessary. (Capsules contain mephenesin and sodium salicylate; tablets and elixir contain in addition homatropine methylbromide).

Detailed information to physicians on request.

CROOKES LABORATORIES, INC.
Therapeutic Preparations for the Medical Profession
MINEOLA, NEW YORK

Crookes

*Patent applied for

Coroner's Corner

Death by Drinking the Most Benign of All Beverages—Milk

Shortly before midnight on one of those hot, sultry nights in August—such as occur annually during that season of the year in the midwest—a transient applied for a single room at a local hotel. The applicant gave his name as Howard Smith; and his address as a town only 20 miles distant from this city. The hotel clerk wondered just why this applicant, whose general appearance and demeanor did not signify opulence, should choose to incur the additional expense of such an obvious luxury item as spending the remainder of the night in a hotel so close to his home. The applicant frankly stated that he had imbibed a considerable quantity of whiskey which might jeopardize his safety in driving those last 20 miles to his home. This logical reason together with the applicant's guileless candor duly impressed the clerk; so after receiving payment in advance for lodging, the key was tendered this slightly inebriated guest.

Before going to his room, Mr. Smith inquired of the clerk as to the location of any nearby store or restaurant at which he might be able to purchase some milk. The clerk stated that no such business establishment within reasonable distance was open at that hour—but that he could spare a couple of quarts of milk from the refrigerator in the hotel kitchen. This transaction was consummated, and Mr. Smith went straightway to his room.

The following morning, the said Mr. Smith failed to appear in the lobby. While doing her routine inspection before beginning her room cleaning, the maid saw exactly why Mr. Smith had failed to respond to her knock on his door. She immediately summoned the manager of the hotel who, in turn, notified the civil authorities.

The Coroner (myself) impaneled a jury and subpoenaed the aforementioned hotel employees as witnesses for an inquest. The facts as related hereabove were affirmed. In the presence of the jury, the coroner pointed out the two empty milk bottles setting on the dresser; next he examined the body of the deceased Mr. Howard Smith and demonstrated the following findings:

(a) Face, lips, and fingers very cyanotic.

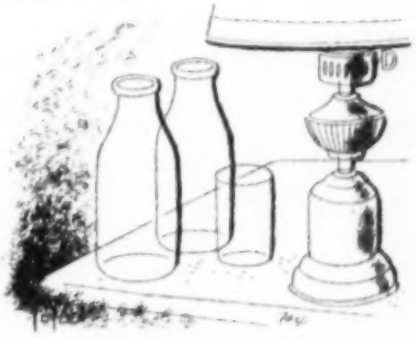
(b) Abdomen grossly distended and very tympanitic.

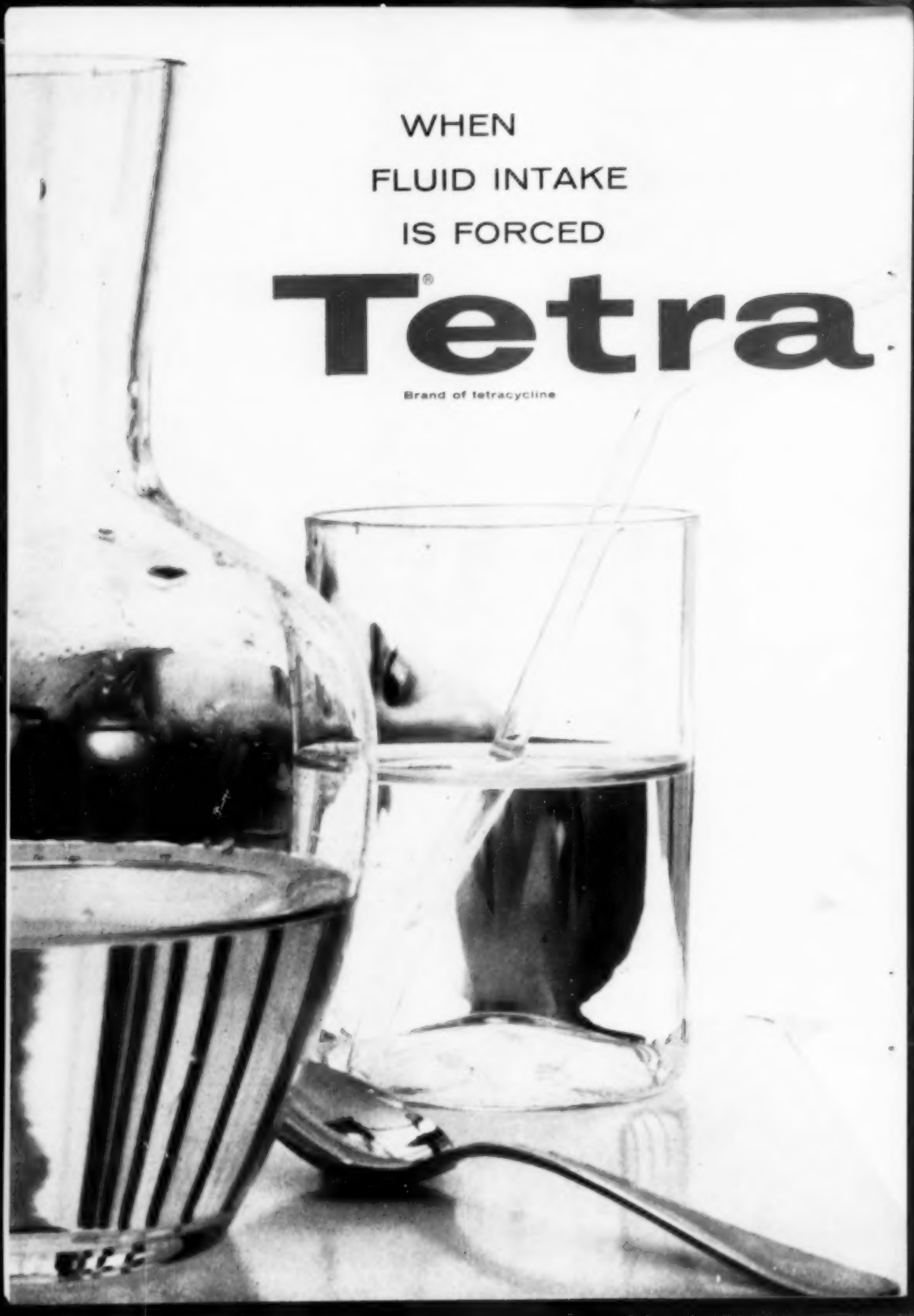
(c) Rigor mortis present only in face (jaws) and neck.

Verdict rendered by coroner's jury is in part as follows: "Because of the ingestion of two quarts of milk, the absorption of the alcohol content of a considerable quantity of whiskey which he had drunk was greatly delayed, thereby giving rise to a tremendous gas pressure in the stomach; this gas pressure in turn impeded the pulsations of the heart to such an extent that circulation was embarrassed sufficiently to be of fatal issue."

Furthermore, the death was adjudged an accident in which the unfortunitous weather conditions played a pertinent contributory role. Because of the intense heat, the unabsorbed milk underwent more rapid decomposition within the tubular confines of Mr. Smith's intestinal tract. Then, in accordance with the laws of physical chemistry, this gas so generated increased in volume in direct proportion to the temperature. The pressure of this gas simultaneously conformed to another scientific law, and finally attained a pressure in the stomach which exerted so great a force that the heart was unable to effectively overcome it and could therefore no longer continue its function.

In summary, Mr. Smith died from the injudicious consumption of milk at the most inopportune time.




WHEN
FLUID INTAKE
IS FORCED
Tetra®
Brand of tetracycline

cyn SF*

provides

DUAL THERAPY

- *controlling effectively a wide variety of pathogenic organisms*
- *supplying and replacing the patient's store of water-soluble vitamins essential for normal resistance and recovery*

maximum antibiotic blood levels[1]
superior clinical effectiveness[2]
superior toleration[3]

with a single prescription

Rx

Tetracyn SF

caps 250 mg.

Available also as oral suspension, containing 125 mg. Tetracyn per 5 cc. teaspoonful.

Terramycin† SF* 250 mg. capsules combine Terramycin with the identical vitamin formula.

The minimum daily dose of each antibiotic furnishes at the same time the vitamin formula recommended by Pollack and Halpern[4] for conditions of stress.

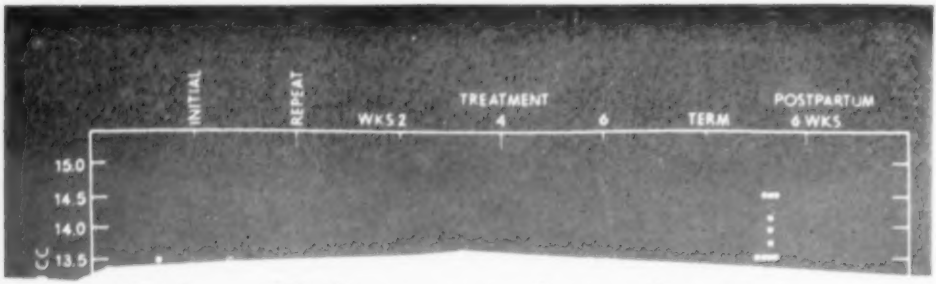
*TRADEMARK FOR PFIZER BRAND OF ANTIBIOTICS WITH VITAMINS

†Brand of oxytetracycline

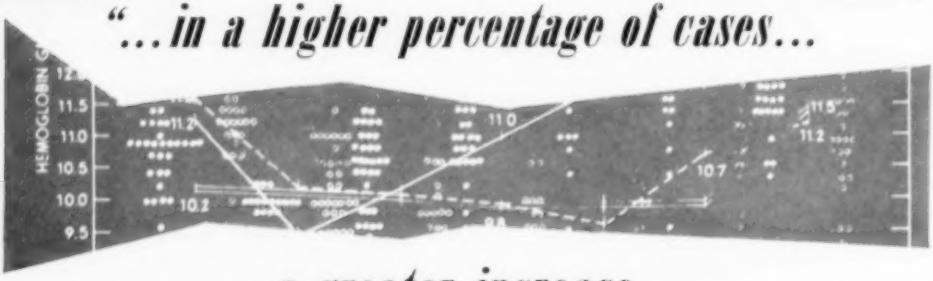
1. Dumas, K. J.; Carlozzi, M., and Wright, W. A.: Antibiotic Med. 1:296 (May) 1955.
2. Prigot, A.: Ann. New York Acad. Sc., in press.
3. Milberg, M. B., and Michael, M., Jr.: Ibid.
4. Pollack, H., and Halpern, S. L.: Therapeutic Nutrition. Prepared in Collaboration with the Committee on Therapeutic Nutrition, Food and Nutrition Board, National Research Council, Washington, D. C., 1952.

Pfizer

PFIZER LABORATORIES, Brooklyn 6, N. Y.
Division, Chas. Pfizer & Co., Inc.

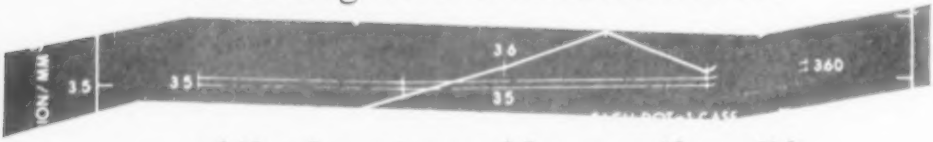


"...in a higher percentage of cases...



...a greater increase

in hemoglobin concentration...



*...with almost no side reactions."**

White's **mol-iron® tablets**

MOLYBDENIZED FERROUS SULFATE

Mol-Iron Liquid Mol-Iron Drops

Forman, J. B.: Anemia of Pregnancy, Connecticut M. J. 14: 930 (Oct.) 1950.
Extensive bibliography on request.

WHITE LABORATORIES, INC., KENILWORTH, N.J.

What's Your Verdict?

Edited by Ann Fidanque, Member of the Bar of New Jersey

On a call from the corporation, the physician attended to one of its employees accidentally injured in the course of employment. The patient indicated that he was injured while tearing down a manhole form used in cement construction. The crowbar he was using slipped, wrenching his body in such a manner as to cause lower back injuries involving the sacroiliac joint. The physician rendered professional care for approximately five months, and then submitted his bill to the corporation. Upon refusal of payment, a court action was instituted.

In avoidance of payment, the corporation counsel alleges that the patient was visited more frequently than necessary, and more particularly that the physician refused to deliver to the corporation for use by other doctors x-ray negatives which had been taken incident to treatment. It is contended that the general rule in respect to ordinary photographs should apply, which gives all property rights in a negative to the one who employs and compensates the photographer in the usual course of business to take the picture.

The physician's attorney contends that x-rays, like microscopic slides of tissue, are a part of the history of the case. In the event of a malpractice suit against a physician or surgeon, the x-ray pictures taken and preserved incident to treatment of the patient might often constitute the unimpeachable evidence justifying the conduct of the physician. The attorney submits that, although the physician refused to surrender possession of the x-ray negatives, he was willing that the negatives should be examined by other physicians if not removed from plaintiff's clinic.

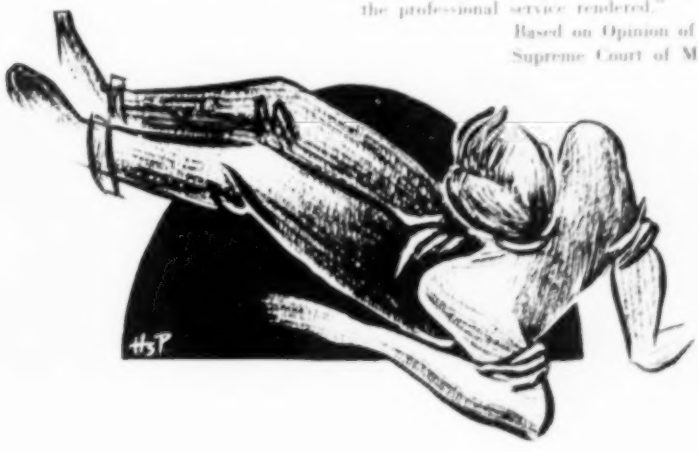
In a nonjury trial before the lower court, the judgment was decided in favor of the physician, from which the defendant appealed. On appeal, what would be your decision?

* * * * *

The Supreme Court of Michigan affirmed the judgment:

"It is a matter of common knowledge that x-ray negatives are practically meaningless to the ordinary layman. But their retention by the physician constitutes an important part of his clinical record in the particular case, and in the aggregate these negatives may embody and preserve much of value incident to a physician's experience. In the absence of an agreement to the contrary, there is every good reason for holding that x-rays are the property of the physician rather than of the patient or party who employed such physician, notwithstanding the cost of taking the x-rays was charged to the patient or to the one who engaged the physician as a part of the professional service rendered."

Based on Opinion of
Supreme Court of Michigan



Pediatrics (child-welfare)*

Upjohn

Gradual and sustained lowering of blood pressure:

Reserpoid

(Pure crystalline alkaloid)

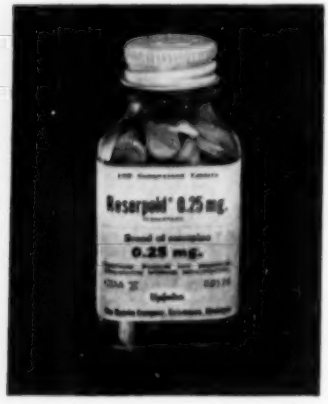
Each tablet contains:

Reserpine ..... 0.1 mg.
or 0.25 mg.
or 1.0 mg.

Supplied:

Scored tablets
0.1 and 0.25 mg. in bottles of 100 and 500
1.0 mg. in bottles of 100

The Upjohn Company, Kalamazoo, Michigan



Romilar 'Roche' a non-narcotic cough specific

Romilar® Hydrobromide -- brand of dextromethorphan hydrobromide

Noludar 'Roche' a mild, non-barbiturate sedative-hypnotic

Noludar® -- brand of methyprylon

Pyelitis (child - 40 lbs.)*

℞ Gantrisin Pediatric Suspension

(acetyl) ℥ iv

S. Initial dose 2 teasp.;

then 1 teasp. q. 6 h.

Daytime Tension

℞ Noludar tabs. 50 mg

#100

S. One tab. 3 times daily

Cough

℞ Romilar tabs. 10 mg

#30

S. One to two tabs.

4 times daily

Acute bronchitis*

℞ Gantrisin tabs. 0.5 Gm

#60

S. 6 tabs. initially; then 4 tabs. q. 6 h.

Nervous insomnia

℞ Noludar tabs. 200 mg

#30

S. One tab. at bedtime

Dry, tracking cough

℞ Romilar Syrup ʒ iv

S. One to two teasp.

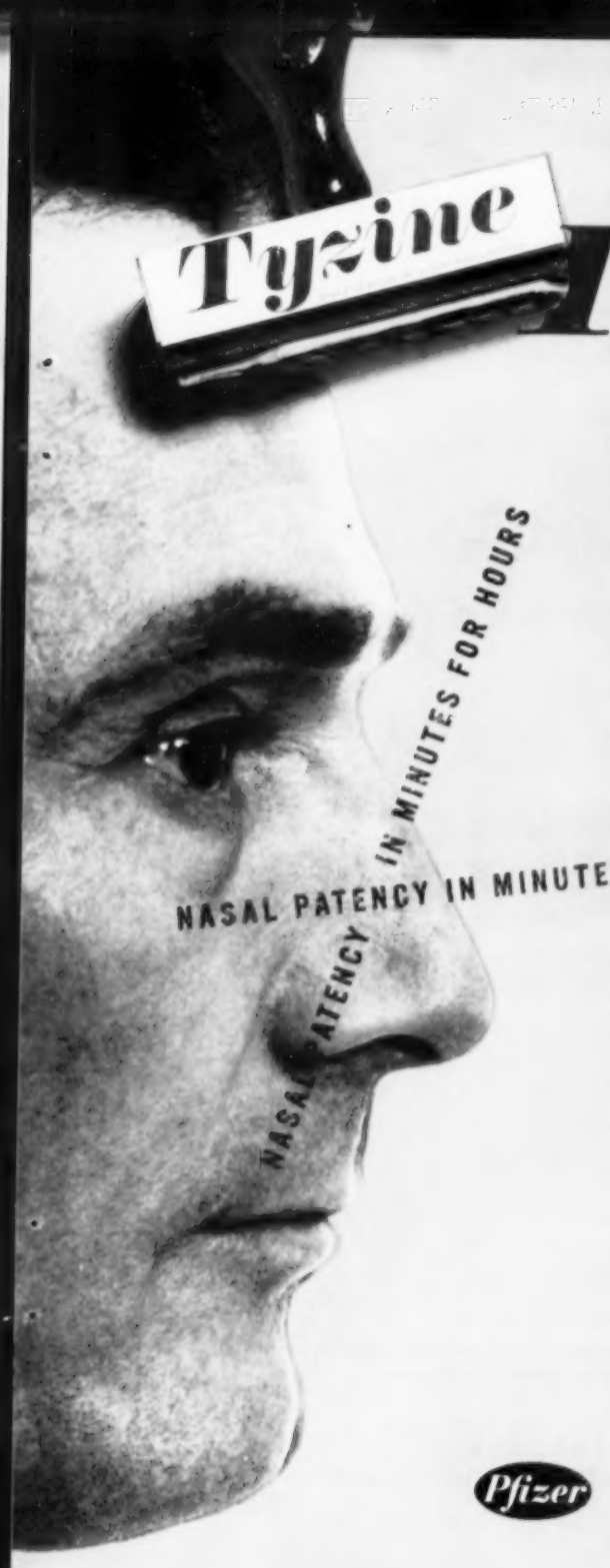
4 times daily

*. . . whom due to susceptible microorganisms. As is true of all antibacterial agents, there may be occasional failures due to resistant strains.

Gantrisin* -- brand of sulfisoxazole

Gantrisin* (acetyl) -- brand of acetyl sulfisoxazole

Gantrisin 'Roche'
a single, soluble, wide-spectrum sulfonamide
Hoffmann - La Roche Inc • Nutley • N.J.



Tyzine®

brand of tetrahydrozoline hydrochloride

nasal spray for impressive results[1,2]

. . . relief for 4 to 6 hours after a single dose . . . and no sting, burn, rebound congestion, or local reactions . . . odorless, tasteless . . . easy to use, convenient to carry in the spill-proof plastic spray bottles.

Supplied: In plastic bottles containing 15 cc., TYZINE, 0.1%.

Also available: TYZINE Nasal Solution, in 1-oz. dropper bottles, 0.1%. TYZINE Pediatric Nasal Drops, in 1/2-oz. bottles, 0.05%, with calibrated dropper for precise dosage.

1. Parish, F. A.: M. Times 82:917, 1954.
2. Menger, H. C.: New York J. Med. 55:812, 1955.

Pfizer

PFIZER LABORATORIES
Division, Chas. Pfizer & Co., Inc.
Brooklyn 6, New York

Preferred for

precision and performance

BARD-PARKER
RIB-BACK
SURGICAL BLADES

It's Sharp

BARD-PARKER RIB-BACK SURGICAL BLADES are preferred by the Profession . . . because they know that each blade, through continuous inspection—meets every specification.

And, there are other traditionally good reasons why there is a preference for B-P RIB-BACK SURGICAL BLADES . . . they are *always* dependable and highly economical in performance.

Ask your dealer

BARD-PARKER COMPANY, INC.
Danbury **Connecticut, U.S.A.**

After Hours

Photographs with brief description of your hobby will be welcomed. A beautiful imported German apothecary jar will be sent to each contributor.

"I find polo a very exciting sport as well as relaxing. Training my own horse to play the game makes this hobby doubly exciting."

Dr. Carl V. Lansing, San Bernardino, California

Dr. Lansing and his daughter, Carla Renee, pictured with their favorite polo pony.

for more "drive"

in tired, run-down, dyspeptic patients

geriatrone
elixir

delightfully flavored digestive-nutritive tonic

	Each fluid ounce (approx. 2 tablespoonfuls) provides: (alcohol 15% by volume)	
digestive enzymes...	Digestive Enzymes:	
	pancreatin	126 mg.
	pepsin	126 mg.
	Betaine HCl	100 mg.
	Betaine Monohydrate	200 mg.
	Liver Concentrate*	220 mg.
lipotropics...	Yeast Extract*	220 mg.
	Vitamin B_{12}	4 mcg.
	Inositol	100 mg.
	Thiamine HCl (B_1)	4 mg.
B complex vitamins...	Riboflavin (B_2)	2 mg.
	Pyridoxine HCl (B_6)	2 mg.
	Panthenol	2 mg.
	Niacinamide	20 mg.
	Calcium Glycerophosphate	300 mg.
	Manganese Glycerophosphate	15 mg.

*provides whole natural vitamin B complex

U | S | V

u. s. vitamin corporation
(ARLINGTON-FUNK LABORATORIES, division)
250 EAST 43rd STREET • NEW YORK 17, N.Y.

for the patient who cannot sleep

To the insomniac, MEDOMIN brings refreshing sleep that is sound, yet not so deep that the patient cannot be awakened if necessary.

The rarity of any undesirable after effects has frequently been noted,[1] and the favorable margin of safety, compared with that of other barbiturates, has been demonstrated in both animals[2] and man.[3]

for the patient who cannot relax

To the patient who cannot relax because of anxiety and nervous tension, MEDOMIN brings a welcome tranquility of mind, a restored ability to sleep through the night, and a gratifying relaxation of tensions.[4]

Medomin®

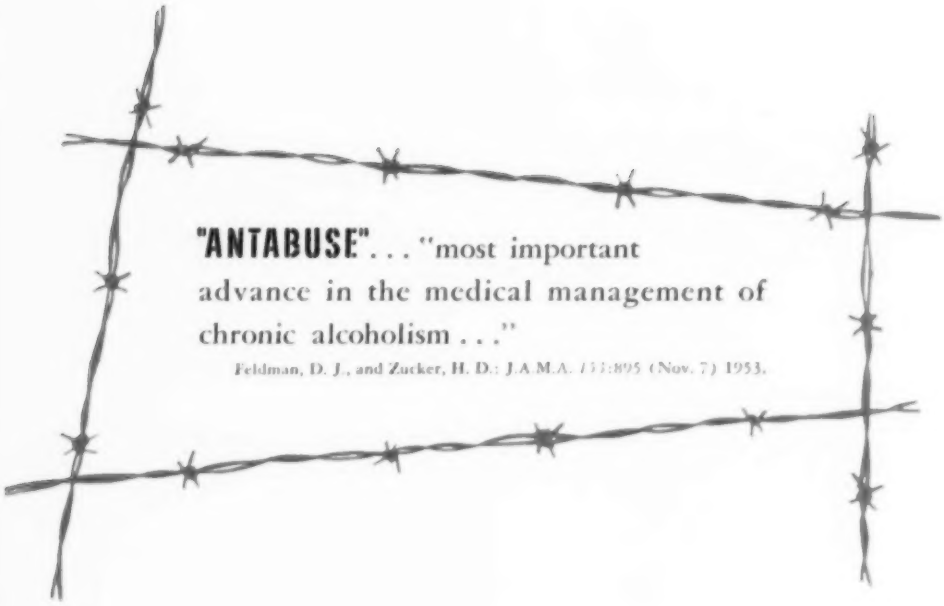
(heptabarbital GEIGY)

Literature and Samples on Request.

MEDOMIN® (brand of heptabarbital). Scored tablets of 50 mg. (pink), 100 mg. (yellow), and 200 mg. (white). Recommended Dosage: As a hypnotic, 200-400 mg.; as a sedative, 50-100 mg. two or three times daily.

References: (1) Brooks, D. D.: J. New. & Ment. Dis. 121:67, 1955. (2) Koppanyi, T., Morgan, C. F., and Pittenger, J. V.: J. Am. Pharm. A. (Scien. Ed.) 44:221, 1955. (3) Fazekas, J. F., and Koppanyi, T.: To be published. (4) Steininger, E.: Psych. Arch. 7:218, 1955.

Geigy GEIGY PHARMACEUTICALS, Division of Geigy Chemical Corporation, 220 Church St., New York 13, N. Y.
In Canada: Geigy Pharmaceuticals, Montreal



A "CHEMICAL FENCE" FOR THE ALCOHOLIC. "Antabuse" gives the patient a forceful and immediate reason for not drinking . . . he finds he cannot drink without experiencing extreme discomfort. By keeping the patient away from alcohol, "Antabuse" serves as a valuable adjunct to psychotherapeutic measures.

"Antabuse"® brand of DISULFIRAM (tetraethylthiuram disulfide) is supplied in 0.5 Gm. tablets, bottles of 50 and 1,000.

Complete information available on request.

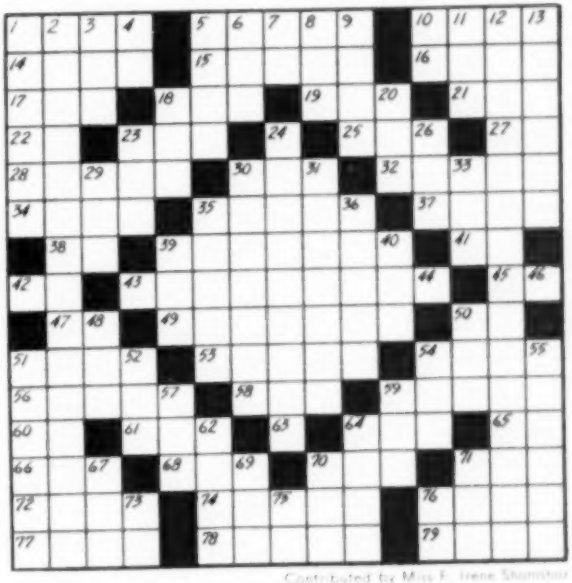
Ayerst Laboratories • New York, N.Y. • Montreal, Canada

5547

MEDICAL TEASERS

A Challenging Crossword Puzzle for the Physician

(Answer on page 42a)



Contributed by Miss F. Irene Shumston

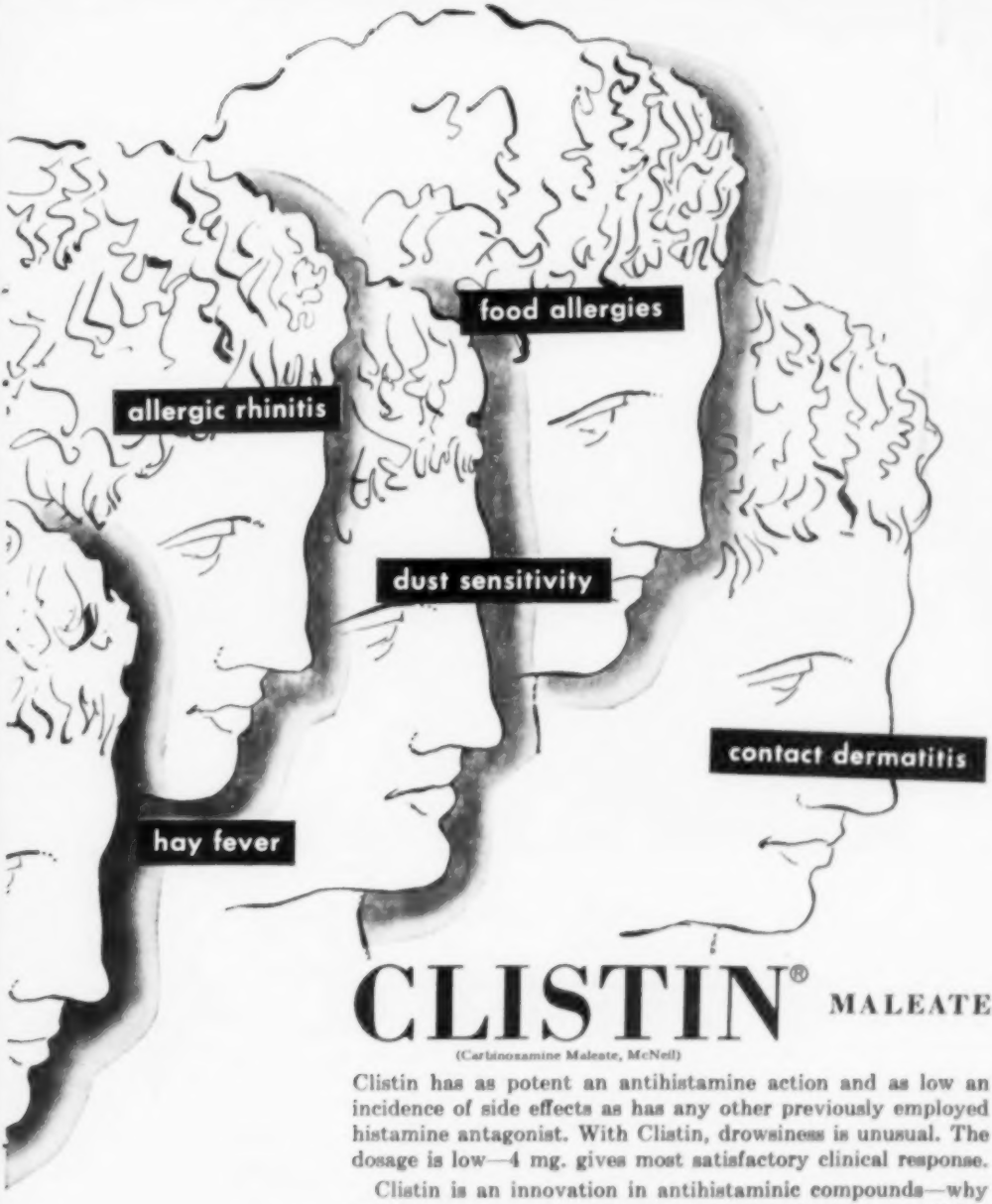
ACROSS

1. Fellow of the American Medical Association
5. A neoplasm
10. One of those killed Cleopatra; probably Cerastes cornutus
14. The first man
15. Lack of muscular coordination
16. Women's Auxiliary Army Corps
17. Pse——— false (prefix)
18. Winglike process
19. Over there!
21. ——ggist, apothecary
22. Symbol of nickel
23. British Broadcasting Corporation (abbr.)
24. Chemical symbol for carbon
25. Definite article
27. Torpedo tubes (abbr.)
28. Analysis of a drug, to determine potency
30. Extinct flightless bird of New Zealand
32. Hiding place
34. Flank
35. Two abbreviations as would be used by the printer to indicate "Paleontology—new paragraph"
37. Regrets
38. Unsatisfactory (colloq.)
39. Upright post to which rope is fastened (naut.)
41. — — T, explosive
42. Bone (Lat.)
43. The clovers; genus of leguminous plants
45. Mouth (Lat.)
47. Chemical symbol for dysprosium
49. Pain-killer
50. Milligram (abbr.)
51. Life (Gk.)
53. French (m.) for 11-down, meaning dismal; depressing
54. Expires
56. Belonging to the god of military prowess and empire
58. A piece of material for use at a door to wipe the shoes on
59. ——— Carta; 1215 A.D.
60. Left eye (abbr.)
61. Milk
63. Chemical symbol for nitrogen
64. A male sheep
65. Mixture of ether and chloroform usually in proportion 16 to 1
66. Any baglike organ
68. Smoked salmon
70. Third person singular of verb "to be" (French)
71. Incombustible mineral residue
72. The sporangia or spore cases of certain lichens and fungi
74. Skin
76. A soft cheese of France ripened by mold
77. A prefix signifying "middle"
78. A feeling of boredom and dissatisfaction
79. A block or form shaped like a foot over which shoe uppers are drawn

DOWN

1. Pertaining to the animal life characteristic of a special location
2. Adrenal insufficiency
3. Master of Obstetric Art (abbr.)
4. Myopic astigmatism (abbr.)
5. Powdered soapstone
6. Skin disease occuring in Peru, resembling Lupus, caused by a species of Leishmania
7. Master of Arts (abbr.)
8. Prefix meaning sharp, quick, or sour
9. India peasant or cultivator of the soil
10. Atomic weight (abbr.)
11. Not happy
12. Asexual reproduction
13. Any squamae or scalelike structures (pl.)
18. ——ss, declivity
20. National Health Council (abbr.)
23. Prohibit
24. A solution of pyroxylin in ether and alcohol used as a protective covering for wounds, burns, ulcers, etc. (var. sp.)
26. The organ of hearing
29. Abbreviation for Latin meaning "let it be labelled"
30. To form abnormally
31. Freudian psychiatrist
33. To incise
35. The tapering end of anything
36. To fix or impress, as a stamp or mark
39. Colloquial for brassiere
40. Owing
42. Symbol for oxygen
43. Time (abbr.)
44. Micrococcus (abbr.)
46. Symbol for sulphur
48. Personal pronoun
50. Russian jet fighter
51. A semifluid, resinous, and fragrant vegetable juice
52. Former name of popular American literary magazine (abbr.)
54. Sheet India rubber used in dentistry and surgery to keep fluids away from the part which is to be operated upon
55. A scent bag
57. Latin for salt
59. Man's nickname
62. Systematic body of law
64. Royal Society of Antiquaries of Ireland (abbr.)
67. Combined Chiefs of Staff (U.S. & Great Britain) (abbr.)
69. Prefix meaning strange, foreign
70. The largest existing bird next to the ostrich
71. ——chnid, spider
73. Chemical symbol for Ionium
75. Registered nurse (abbr.)
76. ——ood, circulating fluid

drug allergies
urticaria



CLISTIN® MALEATE

(Carbinoxamine Maleate, McNeil)

Clistin has as potent an antihistamine action and as low an incidence of side effects as has any other previously employed histamine antagonist. With Clistin, drowsiness is unusual. The dosage is low—4 mg. gives most satisfactory clinical response.

Clistin is an innovation in antihistaminic compounds—why not try it on your next allergy case? Clinical samples available on request.

Dosage forms:
Tablets Clistin Maleate, 4 mg.
Tablets Clistin R-A (repeat action), 8 mg.
Elixir Clistin Maleate, 4 mg. per 5 cc.
Clistin Expectorant
Tablets Clistanal (Clistin Maleate, 2 mg. plus APC)

McNEIL
LABORATORIES, INC.
PHILADELPHIA 32, PA.

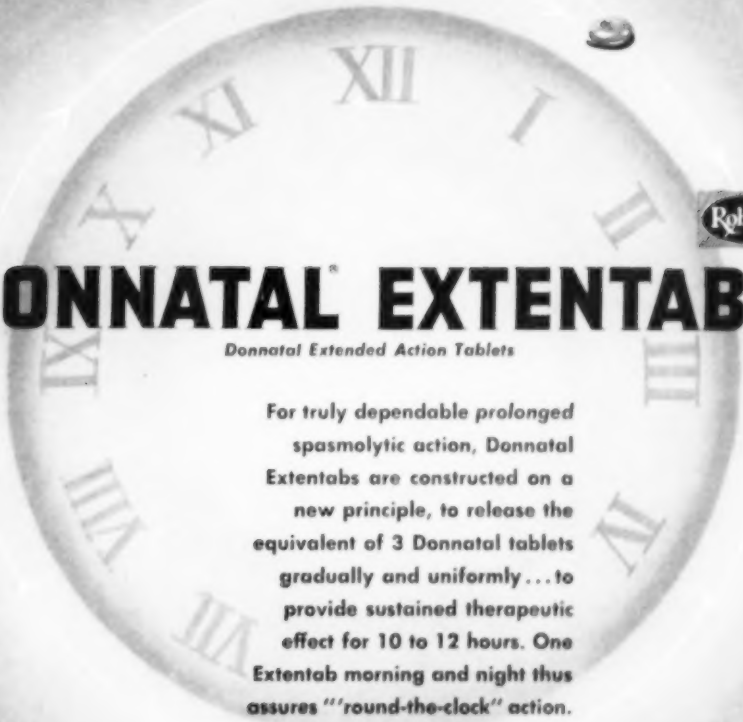
All the body-building nourishment of milk

There's nothing like milk to provide the nutrients needed for steady growth . . . and when you recommend Pet Evaporated Milk, you know that babies in your care are getting *all* of the nourishment the best milk can be depended on to supply . . . and these food values are *always* uniform in composition and quality wherever and whenever low-cost Pet Milk is obtained.

Favored Form of Milk
For Infant Formula

PET MILK COMPANY, ARCADE BUILDING, ST. LOUIS 1, MO.

NOW—for p-r-o-l-o-n-g-e-d spasmolytic action—



Robins

DONNATAL® EXTENTABS®

Donnatal Extended Action Tablets

For truly dependable *prolonged* spasmolytic action, Donnatal Extentabs are constructed on a new principle, to release the equivalent of 3 Donnatal tablets gradually and uniformly . . . to provide sustained therapeutic effect for 10 to 12 hours. One Extentab morning and night thus assures "round-the-clock" action.

Each Donnatal Extentab contains:

Hyoscyamine Sulfate	0.3111 mg.
Atropine Sulfate	0.0582 mg.
Hyoscine Hydrobromide	0.0195 mg.
Phenobarbital (¼ gr.)	48.6 mg.

Also available **DONNATAL**
tablets, capsules and elixir

A. H. ROBINS CO., INC. • RICHMOND 20, VA.

Ethical Pharmaceuticals of Merit since 1878

® Trade Mark

NEW! ACHROMYCIN OPHTHALMIC OINTMENT *with* HYDROCORTISONE

(Tetracycline 1%, Hydrocortisone 1.5%)

Lederle's versatile broad-spectrum antibiotic and hydrocortisone, an established anti-inflammatory agent, are now combined in a lanolin-petrolatum base. This dual-action ointment is useful in treating a wide variety of ocular infections, and many noninfectious eye conditions, including corneal injuries.

Package: ¼ oz. collapsible tube.

Other forms of ACHROMYCIN for ophthalmic use:

Ophthalmic Ointment 1%: ¼ oz. tube.

Ophthalmic Solution: vial of 25 mg. with sterilized dropper vial.

ACHROMYCIN*

TETRACYCLINE *LEDERLE*

Lederle

LEDERLE LABORATORIES DIVISION *American Cyanamid Company* Pearl River, New York

*Reg. U.S. Pat. Off.

for "This Wormy World"

SYRUP TABLETS

'ANTEPAR'*

effective against

PINWORMS
and
ROUNDWORMS

'Antepar' is well-tolerated and pleasant to take.

'SYRUP OF 'ANTEPAR' Citrate brand Piperazine Citrate, containing the equivalent of 100 mg. piperazine hexahydrate per cc.

Bottles of 4 fluid ounces, 1 pint and 1 gallon.

'TABLETS OF 'ANTEPAR' Citrate brand Piperazine Citrate, available in two strengths equivalent to either 250 mg. or 500 mg. piperazine hexahydrate, scored.

Bottles of 100

BURROUGHS WELLCOME & CO. (U.S.A.) Inc., *Tuckahoe 7, N. Y.*

BLUE
AT
BREAKFAST?

BONADOXIN*

(BRAND OF MECLIZINE HCl, PYRIDOXINE HCl)

stops morning sickness

RESULTS
of
this
new
COMBINATION

In 100 patients with severe nausea and vomiting, Weinberg reports 88% good to excellent results.[1] In another series, BONADOXIN abolished vomiting in 40 of 41 gravida, eliminated nausea in 30 of the 41.[2]

Each BONADOXIN tablet contains:

MECLIZINE HCl	25 mg.
PYRIDOXINE HCl	50 mg.

Mild cases: One BONADOXIN tablet at bedtime.
Severe cases: One at bedtime and on arising.
In bottles of 25 and 100, prescription only.
Also indicated in post-radiation sickness, nausea following surgery, Ménière's syndrome.

Rx PFIZER

Chicago 11, Illinois

*TRADEMARK

1. Weinberg, Arthur and Werner, W. E. F.: Bonadoxin, a new effective oral therapy for hyperemesis gravidarum. Am. Pract. and Dig. of Treatment. In press. 2. Personal communication. 3. Berenson, F.: Bonadoxin: oral therapy for nausea and vomiting of pregnancy. In press.

Advertisement

LETTERS TO THE EDITOR

This department is offered as an Open Forum for the discussion of topical medical issues. All letters must be signed. However, to protect the identity of writers, who are invited to comment on controversial subjects, names will be omitted when requested.

More on Prescription Pad Holders

Just received your beautiful gift. I put everything aside just to write you these few words to thank you from the bottom of my heart.

I must again repeat that MEDICAL TIMES is the magazine for the G.P. Concise and to the point.

Again let me thank you.

B.E., M.D.
Brooklyn, New York

I consider myself fortunate to be on your mailing list for MEDICAL TIMES which I consider to be a very fine journal with excellent, well-written articles that keep the G.P. well informed.

I am writing to request one of the prescription pad holders and wallets which you mentioned were available to any physician on the MEDICAL TIMES mailing list as mentioned in the July issue.

L.P.J., M.D.
Duquesne, Penna.

—Concluded on page 51a

Anti-asthmatic

Quadrinal tablets

QUADRINAL TABLETS CONTAIN FOUR DRUGS, EACH SELECTED FOR ITS PARTICULAR EFFECT IN CHRONIC ASTHMA AND RELATED ALLERGIC RESPIRATORY CONDITIONS.

℞ ½ or 1 Quadrinal Tablet every 3 or 4 hours, not more than three tablets a day.

Each Quadrinal Tablet contains ephedrine hydrochloride ⅜ gr. (24 mg.), phenobarbital ⅛ gr. (24 mg.), Phyllicin (theophylline-calcium salicylate) 2 gr. (120 mg.), and potassium iodide 5 gr. (0.3 Gm.).

Quadrinal Tablets are marketed in Bottles of 100, 500 and 1000.

Quadrinal, Phyllicin, Trademarks R. Bilhuber, Inc.

BILHUBER-KNOLL CORP.
Orange, New Jersey, U. S. A.

When Authorities Agree

THE ADVANTAGES and merits of a therapeutic substance can be properly evaluated from the *latest* medical literature. In the light of studies in recent years, phenolphthalein emerges as the laxative of choice for relief of occasional constipation and the more prolonged treatment of chronic intestinal stasis.

The gentle action of phenolphthalein is acknowledged by such authorities as Sollmann[1] who describes it as "mild." Goodman and Gilman[2] state that its action "is not accompanied by colic or intestinal griping." Krantz and Carr[3] designate phenolphthalein as "one of the most popular cathartic drugs" because of its "mild cathartic action." Beckman[4] considers phenolphthalein "a very reliable cathartic for use at bedtime to produce a stool much like the normal in the morning," and so safe that "infants of 18 months may be given as much as 30 mg. (½ grain)," which is one-half of the U.S.P. adult dose. The wide use of phenolphthalein is attributed to its "palatability and apparent safety" in the Collaborative Textbook edited by Drill.[5]

Another outstanding advantage of phenolphthalein is the freedom it assures from secondary constipation. The initial action is followed by an aperient effect for two to four days.[1,2,3,6] This "tonic" influence[7] gently stimulates peristaltic action and enables the colon to resume its previous normal functioning.

The phenolphthalein used in Ex-Lax is biologically standardized for uniform efficiency. The chocolated base imparts unusual palatability, making Ex-Lax especially suitable for use when taste requires particular consideration, as during pregnancy and in administration to children.

A liberal trial supply of Ex-Lax, and a Physician's Pocket Notebook, bound in leather, stamped in gold, and making medical reference information readily available, gladly sent to physicians. Ex-Lax, Inc., Brooklyn 17, New York.

1. T. Sollmann: A Manual of Pharmacology. W. B. Saunders Co., 1948; page 177.
2. L. Goodman and A. Gilman: The Pharmacologic Basis of Therapeutics. The Macmillan Co., 1941; p. 823.
3. J. C. Krantz, Jr. and C. J. Carr: The Pharmacologic Principles of Medical Practice. The Williams and Wilkins Co., 1951; page 377.
4. H. Beckman: Pharmacology in Clinical Practice. W. B. Saunders Co., 1952; page 369.
5. V. A. Drill, ed.: Pharmacology in Medicine. McGraw-Hill Book Co., 1954; page 44/7.
6. S. Ditkowsky and F. Steigmann: J. Pediat. 45:169, August, 1954.
7. A. Grollman: Pharmacology and Therapeutics. Lea and Febiger, 1954; page 391.

Now...
Available on your prescription

NEWEST
ANTI-RHEUMATIC

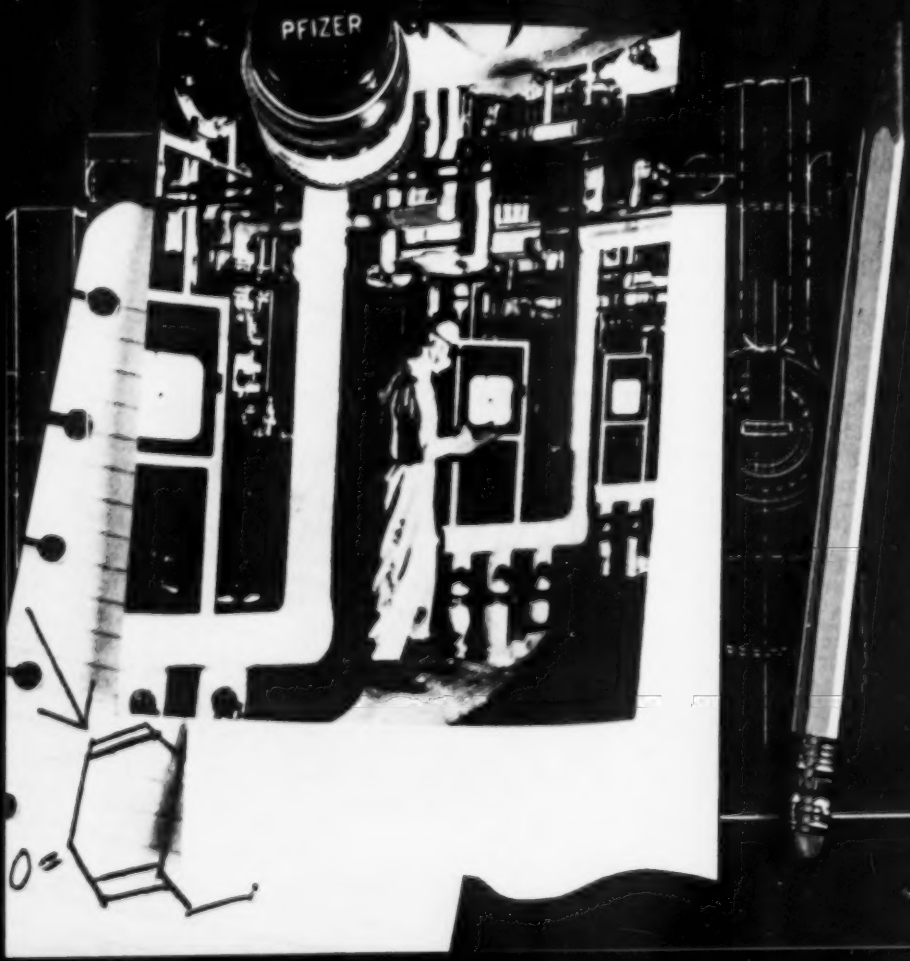
announcing the

NEWEST

highly potent

Anti-rheumatic

Ste



REFERENCES:

rane*

intensified potency[1-6]

3 to 5 times more potent than cortisone or hydrocortisone

notable absence of major side effects[1-3, 6]

virtually without edema caused by sodium and water retention—avoids excessive potassium loss—other side reactions usually minor and frequently transient

rapid improvement in rheumatoid arthritis[1]

prompt relief of subjective and objective symptoms—Sterane has also shown excellent clinical response in bronchial asthma and inflammatory skin conditions

anti-inflammatory anti-rheumatic anti-allergic

Supplied as scored 5 mg. oral tablets, shaped like the familiar Pfizer oval. Bottles of 20 and 100.

1. Bunim, J. J., et al.: J.A.M.A. 157:311, 1955. 2. Boland, E. W.: California Med. 82:65, 1955. 3. Norred, S. R.: Am. Prof. Pharm. 21:241, 1955. 4. Waine, H.: Bull. Rheumat. Dis. 5:81, 1955. 5. Herzog, H. L., et al.: Science 121:176, 1955. 6. Spies, T. D.: GP, in press.

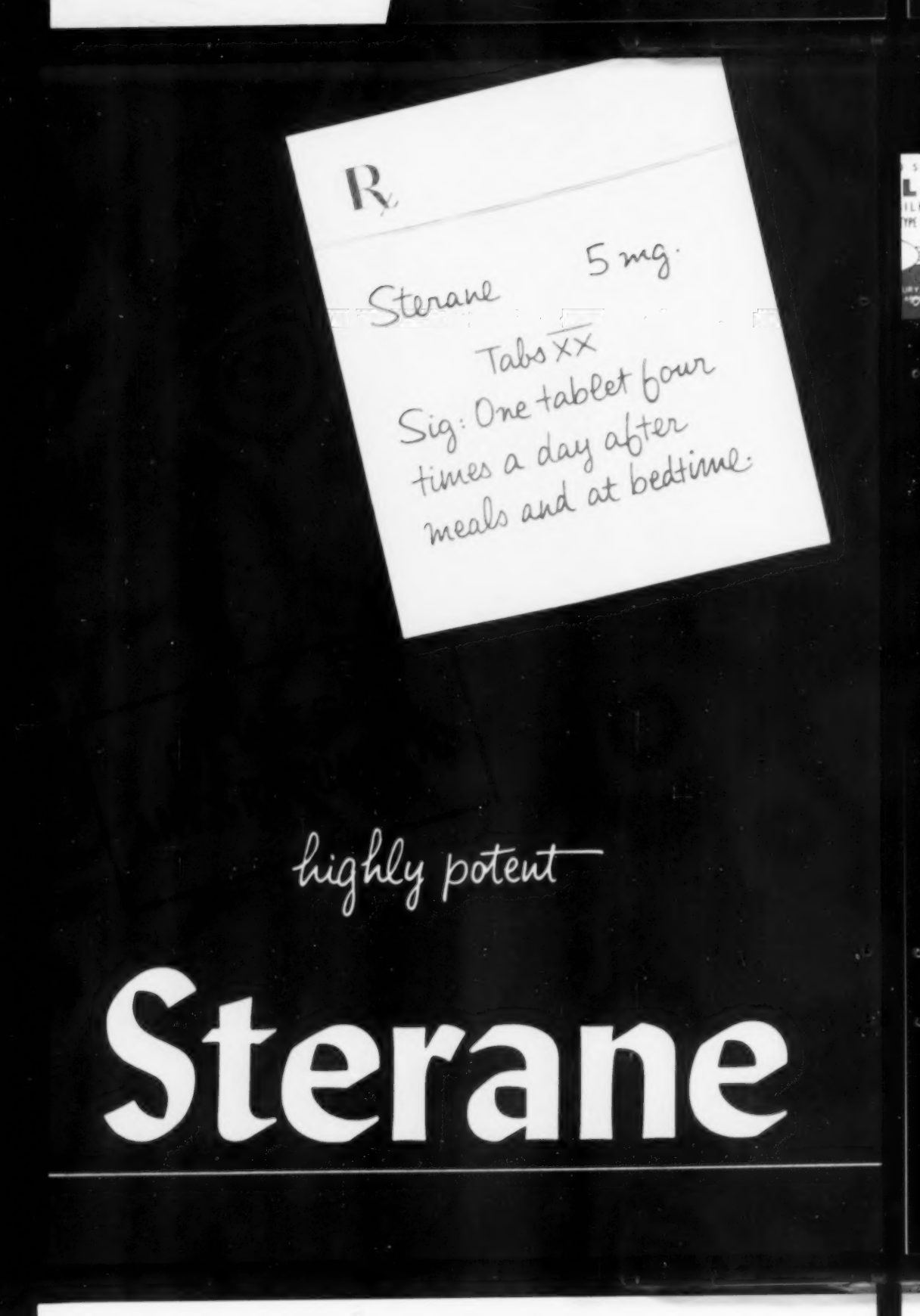
PFIZER LABORATORIES

Division, Chas. Pfizer & Co., Inc.

Brooklyn 6, New York

STERANE TABLETS

* brand of prednisolone


℞
Sterane 5 mg.
Tabs XX
Sig: One tablet four times a day after meals and at bedtime.
highly potent
Sterane

reduces handling

costs no more than spools

sutures always protected and identified

in tape-measure dispensing package

20 strands to cut to any length with a single snip

D&G MEASUROLL®

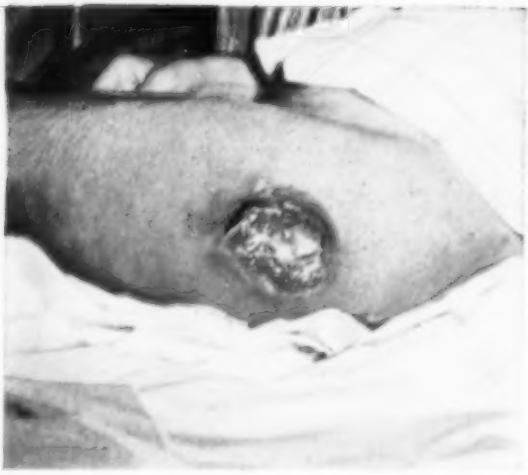
SILK*
COTTON

*Anacap® brand

DAVIS & GECK INC.
A unit of American Cyanamid Company
DANBURY, CONNECTICUT

Effective local treatment

FOR BEDSORES AND OTHER CHRONIC ULCERATIONS



May 15th. Severe decubitus ulcer over femoral greater tuberosity in a terminally ill patient.

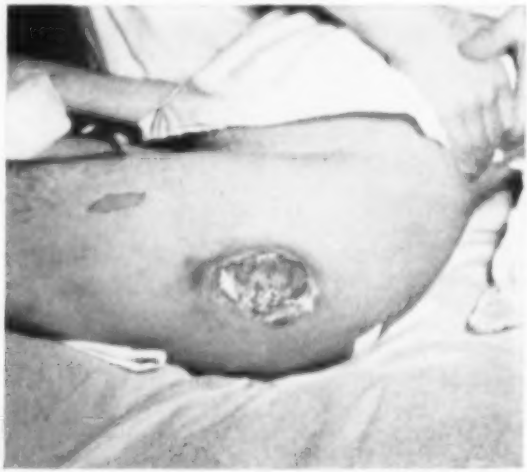
WHITE'S VITAMIN A & D OINTMENT

Routine application of White's Vitamin A & D Ointment promotes granulation and epithelization in *stubborn bedsores, chronic ulcers of varied etiology, burns and slow-healing wounds* that do not permit primary surgical closure. It is also useful as a protective and therapeutic covering in miscellaneous skin conditions characterized by abnormal dryness. White's Vitamin A & D Ointment provides vitamins A and D in a pleasant lanolin-petrolatum base that does not stain tissues or bed clothes.

℞ in 1½ oz. or 4 oz. tubes; 1 lb. or 5 lb. jars.

White's

WHITE LABORATORIES, INC., KENILWORTH, N. J.



July 12th. After 2 months of treatment with White's Vitamin A & D Ointment, ulcer crater reveals healthy granulation tissue and evidence of beginning epithelial repair.

LETTERS TO THE EDITOR

—Continued from page 49

A rather belated note to tell you that I appreciated very much the prescription pad and wallet. Also to tell you that I enjoy MEDICAL TIMES very much. Of all the journals I receive I really get more out of MEDICAL TIMES than most any of them. The articles are brief, concise and to the point. It isn't necessary to do so much reading of details.

D.B.R., M.D.
Cullman, Alabama

Since your publication has been coming each article that especially concerns G.P. practice has been read.

Then one day you sent the leather case for R pad and that's supurb—no more dog ears on the prescriptions. I took mine to the shoe shop and had a leather pocket stitched in to slip my pencil in. Some of your other readers might be interested in the suggestion.

F.G.F., M.D.
Houston, Texas

Like MT

I enjoy your concise articles every month and pass the journal on to the others on our staff. I do hope you keep on sending it.

G.O.G., M.D.
Boulder, Colorado

Your journal is awaited each month with enthusiasm.

The refresher article and the clinico-pathological conferences are the first to get my attention.

Thank you for an interesting and up-to-date journal for the busy practitioner.

S.L.A., M.D.
Hampton, Virginia

For Prompt Relief From Nasal Congestion Prescribe

EFEDRON HYDROCHLORIDE* NASAL JELLY

RAPID relief is assured because the bland, water soluble base of Efedron is miscible with nasal secretion, insuring immediate therapeutic action.

PROLONGED shrinkage is attained by the viscous consistency of Hart Nasal Jelly (Efedron) which affords a more extended contact with the mucosa than a purely liquid form.

SAFETY from the danger of respiratory irritation and lack of appreciable interference with ciliary activity characterize Efedron because it is water soluble.

CONVENIENT, easy-to-carry and to use, handy in purse or pocket. No messy drops or spillage.

CHILDREN accept it readily, because of its handy form and the pleasant, soothing relief it affords.

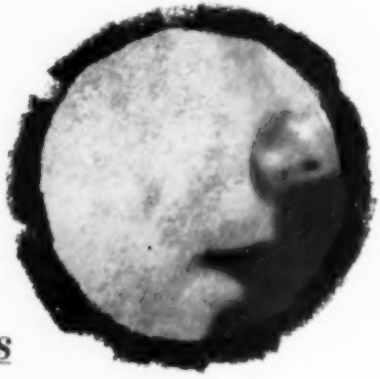
TIME-TESTED and proven over the years, Efedron enjoys the nation-wide acceptance that befits a *dependable* product offered at an *economical* price.

**Brand of Ephedrine Hydrochloride*

HART DRUG CORPORATION
MIAMI, FLORIDA

A 19 year old female with a 5 year history of cystic pustular scarring acne of face and back refractory to all other types of therapy.

After 12 weeks of treatment with "Premarin" Lotion applied to face only, remission is apparent. Untreated back remains unchanged.



Excellent results obtained

in acne vulgaris

with "Premarin®" Lotion

Conjugated Estrogens (equine) for topical application

The case illustrated above is typical of the response obtained with "Premarin" Lotion in 70 to 80 per cent of patients of both sexes with refractory chronic acne of the cystic and pustular types.[1] "Premarin" Lotion was found particularly suitable because it provides concentration of medication at site of desired action; permits dosage control to eliminate possibility of side effects; and is esthetically acceptable to both male and female patients.

also effective in seborrheic alopecia

Within three to six weeks, control of scaling and itching and reduction of hair loss, particularly about the vertex of the scalp, were noted following application of "Premarin" Lotion, two or three times a day. No systemic effects were noted.[2]

Supplied: No. 875—Bottles of 60 cc. with applicator. Each cc. contains 1 mg. of estrogens in their naturally occurring, water-soluble conjugated form expressed as sodium estrone sulfate.

Detailed information available upon request.

1. Shapiro, I.: Postgrad. Med. *15*:503 (June) 1954; J. M. Soc. New Jersey *52*:6 (Jan.) 1955.

2. Shapiro, I.: J. M. Soc. New Jersey *50*:17 (Jan.) 1953.

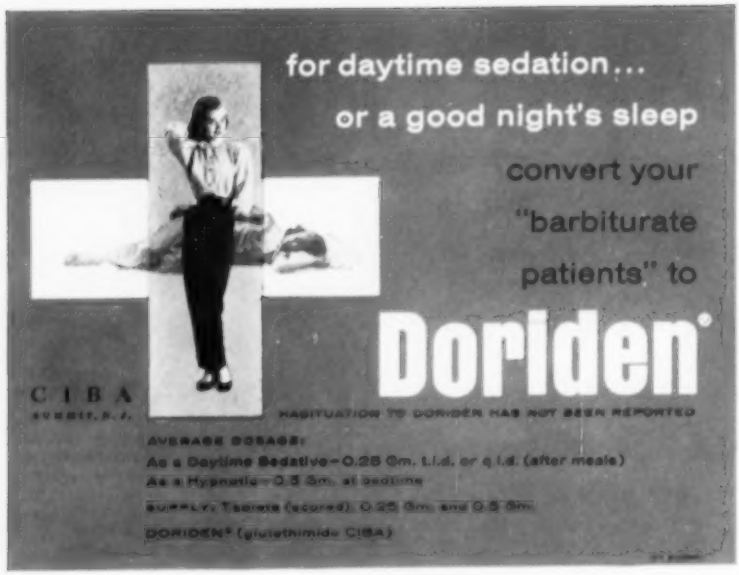
Ayerst Laboratories • New York, N. Y. • Montreal, Canada

5544

Burger Bill is Vitamin-Nil

Funny thing about Bill. He grew up, but his appetite didn't. Not that hamburgers aren't nourishing; but with Bill, it's burgers for lunch, burgers for dinner, and burgers in between. Like other Dietary Dubs, he'll soon need your help. A balanced, varied diet, obviously. And for potent, multivitamin support—a DAYALET a day. Abbott

give him
a Dayalet®
a Day


for daytime sedation...
or a good night's sleep
convert your
"barbiturate
patients" to
Doriden®
CIBA
HABITUATION TO DORIDEN HAS NOT BEEN REPORTED
AVERAGE DOSAGE:
As a Daytime Sedative—0.25 Gm. t.i.d. or q.i.d. (after meals)
As a Hypnotic—0.5 Gm. at bedtime
SUPPLY: Tablets (scored), 0.25 Gm. and 0.5 Gm.
DORIDEN® (glutethimide CIBA)

MODERN MEDICINALS

These brief resumes of essential information on the newer medicinals, which are not yet listed in the various reference books, can be pasted on file cards and a record kept. This file can be kept by the physician for ready reference.

Ambar Extentabs, A. H. Robins Co., Inc., Richmond 20, Virginia. Each Extentab contains methamphetamine hydrochloride 10.0 mg., phenabarbital 64.8 mgm. Constructed so that one-third of the contents mentioned above is released for immediate action and the remaining two-thirds are released gradually and uniformly. A superiod psycho-normalizer. **Dose:** One or two Extentabs before breakfast. **Sup:** Bottles of 100 and 500.

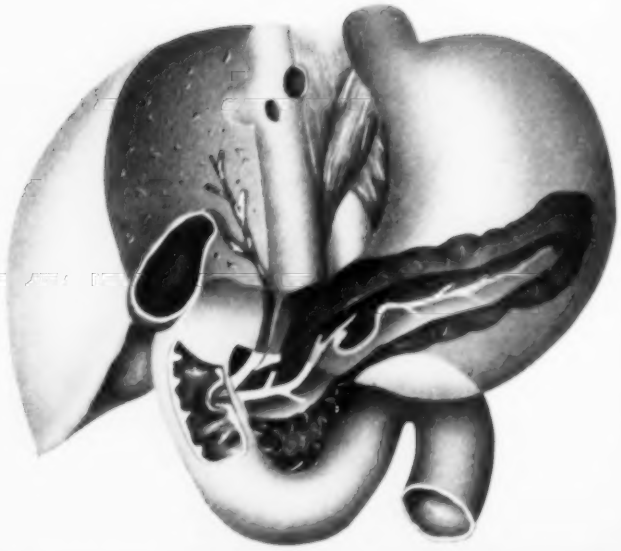
Ambar Tablets, A. H. Robins Co., Inc., Richmond 20, Virginia. Each tablet contains methamphetamine 3.33 mg., phenobarbital 21.6 mgm. Recommended for the amelioration or relief of the manifold symptoms attending tension, anxiety and fatigue states. **Dose:** One or two tablets taken before breakfast and lunch and in mid-afternoon. **Sup:** In bottles of 100 and 500 tablets.

Cortisporin Antibiotic Ointment, Burroughs Wellcome & Co., Inc., Tuckahoe 7, New York. Each gram contains Aerosporin Sulfate Polymyxin B Sulfate 5,000 Units; bacitracin 400 Units, neomycin sulfate 5 mg., hydrocortisone 10 mg. Topical and Ophthalmic. Inflammatory conditions of the skin and anterior segment of the eye, which are associated with bacterial infection are indications for Cortisporin. The Ointment is also of value for inflamed lesions which are not infected but which it is desired to protect against bacterial infections. In this group conditions of allergic etiology are of particular interest. **Dose:** As determined by physician. **Sup:** In tubes containing 1/8 ounce.

Deltasone, The Upjohn Company, Kalamazoo, Michigan. New, synthetic steroid producing effects similar to cortisone but 3 to 5 times as potent. Small, scored, flat-surfaced tablets in 5 mg. strength with the generic name prednisone. To date used mainly in treatment of rheumatoid arthritis and intractable bronchial asthma. After final clinical confirmation, expected to be effective in same conditions for which cortisone is now indicated. **Dose:** Orally, as determined by physician. **Sup:** In bottles of 30, 100, 500 and 1,000 tablets.

Hollandex Silicone, Holland-Rantos Co., Inc., New York 13, New York.

Continued on page 60a



constipation
and
related
functional
G. I. distress

markedly relieved in
8 out of 10 patients*
by inexpensive, physiologic
stimulant

DECHOLIN® with Belladonna

improved liver function* PLUS *reliable spasmolysis

Steps up flow of dilute bile by *hydro*choleresis • physiologic elimination without catharsis • relieves spasm • no cramping • no evidence of tolerance • helps establish normal bowel habits

One or, if necessary, two *Decholin*/Belladonna Tablets t.i.d. gives your patients more effective relief of constipation and related G.I. complaints: flatulence, bloating, belching, nausea and indigestion.

Each tablet contains *Decholin* (dehydrocholic acid, *Ames*) 3¾ gr., and extract of belladonna ⅛ gr. (equivalent to tincture of belladonna, 7 minims). Bottles of 100 and 500.

*King, J. C.: Am. J. Digest. Dis. 22:102, April, 1955.

AMES
COMPANY, INC • ELKHART, INDIANA • Ames Company of Canada, Ltd., Toronto

Pyridium®

(PHENYLAZO-DIAMINO-PYRIDINE HCl)

Gratifying relief from urogenital symptoms *in a matter of minutes*

MAJOR ADVANTAGES: Nontoxic, soothing urinary analgesic. Rapid and entirely local action. Compatible with sulfas and antibiotics.

FOR COMFORT
ON THE JOB . . . AND AT PLAY

EFFECTIVE In one series of cases of pyelonephritis, cystitis, prostatitis and urethritis, PYRIDIUM decreased pain and burning in 93% of the patients and promptly relieved urinary frequency in 85% of cases.[1]

WELL-TOLERATED Specific local analgesic action is confined to the urogenital mucosa. PYRIDIUM may be administered concomitantly with the sulfonamides or antibiotics to provide relief from pain in the interval before the antibacterials can act.

PHYSIOLOGICAL The soothing analgesic action contributes to relaxation of the sphincters of the bladder, thus promoting complete emptying at each micturition.

PSYCHOLOGICAL To the patient, the rapid appearance of the orange-red color is tangible evidence of the prompt action of PYRIDIUM.

SUPPLIED in 0.1 Gm. (1½ gr.) tablets, in vials of 12 and bottles of 50, 500 and 1000.

PYRIDIUM is the registered trade-mark of Nepera Chemical Co., Inc. for its brand of phenylazo-diamino-pyridine HCl. Sharp & Dohme, Division of Merck & Co., Inc., sole distributor in the United States.

SHARP & DOHME
PHILADELPHIA 1, PA.
DIVISION OF MERCK & CO., INC.

REFERENCE: 1. Kirwin, T. J., Lowsley, O. S., and Menning, J.: Am. J. Surg. **62**:330-335, December, 1943.

—Continued from page 57a

Dermatological ointment. Formula: Silicone ointment with vitamins A and D as contained in natural cod liver oil; water-repellent. For chaffing, diaper rash, minor skin irritations, etc.; as a multi-use skin medicament. **Dose:** As determined by physician. **Sup:** In one-ounce and two and three-fourth ounce tubes.

Hydeltra Tablets, Sharp & Dohme, Inc., Division of Merck & Co., Inc., Philadelphia 1, Pennsylvania. Each tablet is scored and contains 5 mg. of prednisolone, A synthetic analogue of hydrocortisone with similar but more potent therapeutic anti-inflammatory action. **Dose:** As determined by physician. **Sup:** In bottles of 30 and 100 tablets.

Hydrospray Nasal Suspension, Sharp & Dohme, Inc., Division of Merck & Co., Inc., Philadelphia 1, Pennsylvania. In each cc.: Hydrocortone 1 mgm., propadrine Hcl., 15 mgm., neomycin sulfate, 5 mgm. Anti-allergic, anti-inflammatory, decongestant, anti-infective. For allergic rhinitis, hay fever, vasomotor rhinitis. **Dose:** As determined by physician. **Sup:** In bottles of 15 cc.

Merlenate, Chicago Pharmacal Company, Chicago, 40, Illinois. Ointment, powder: dermatological/fungicidal. Each ounce contains undecylenic acid 5%; phenylmercuric nitrate 1:1500. For athlete's foot and other common, superficial fungous infections of the skin. **Dose:** After cleaning and drying

—Continued on page 66a

Angina pectoris prevention

Most efficient of the new long-acting nitrates, METAMINE prevents angina attacks or greatly reduces their number and severity. Tolerance and methemoglobinemia have not been observed with METAMINE, nor have the common nitrate side effects such as headache or gastric irritation. Dose: 1 or 2 tablets after each meal and at bedtime. Also: METAMINE (2 mg.) with BUTABARBITAL (¼ gr.), bottles of 50. THOS. LEEMING & CO., INC., 155 EAST 44TH STREET, NEW YORK 17, N.Y.

unique amino nitrate

Metamine

triethanolamine trinitrate biphosphate, Leeming, tablets 2 mg. Bottles of 50 and 500

invitation to asthma?

not necessarily . . .

Tedral, taken at the first sign of attack, often forestalls severe symptoms.

- ***relief in minutes***...Tedral brings symptomatic relief in a matter of minutes. Breathing becomes easier as Tedral relaxes
- smooth muscle, reduces tissue edema, provides mild sedation.

for 4 full hours...Tedral maintains more normal respiration for a sustained period—not just a momentary pause in the attack.

Tedral provides:

Theophylline	2 gr.
Ephedrine HCl	3/8 gr.
Phenobarbital	1/8 gr.

in boxes of 24, 120 and 1000 tablets

Tedral®

WARNER-CHILCOTT

Now! twice a day dosage

results in therapeutic **sulfonamide** blood levels

Lipo-Triazine*

brand of meth-dia-mer sulfonamides

- **better patient cooperation from twice a day dosage**
- **better dosage control from twice a day dosage**
- **greater relative safety**

also available

Lipo-Diazine*

(brand of sulfadiazine)

Bottles of 4 and 16 oz.

"Sulfonamides in an oral fat emulsion vehicle are absorbed to higher and more prolonged blood levels in experimental animals and human subjects, as compared with absorption from an aqueous vehicle."

Stephens, L. J., and Hendrickson, W. E.:
To be published.

Literature and samples on request.

DONLEY-EVANS & COMPANY ST. LOUIS 15, MISSOURI

The originators of liquid sulfa

*Exclusive trademarks of Donley-Evans & Co.; subjects to patents pending

Safer Combination Therapy

IN

HYPERTENSION

Rauwiloid® + Veriloid®

in a single tablet

Indicated in moderately severe hypertension. Each tablet contains 1 mg. Rauwiloid and 3 mg. Veriloid.

Initial dosage, one tablet t.i.d., p.c. Available in bottles of 100 tablets.

- SIMPLER THERAPY—Simplified dosage regimen, simplified dosage adjustment, and easier patient management.
- GREATER SAFETY—GREATER EFFICACY—Under the synergistic influence of Rauwiloid, the potent antihypertensive agents act with greater efficacy at lower, better tolerated dosages, notable freedom from chronic toxicity.
- BETTER PATIENT COOPERATION—In each instance, only one medication to take . . . hence easier-to-follow dosage instructions.

Rauwiloid® + Hexamethonium

in a single tablet

Indicated in rapidly progressing, otherwise intractable hypertension. Each tablet contains 1 mg. Rauwiloid and 250 mg. hexamethonium chloride dihydrate.

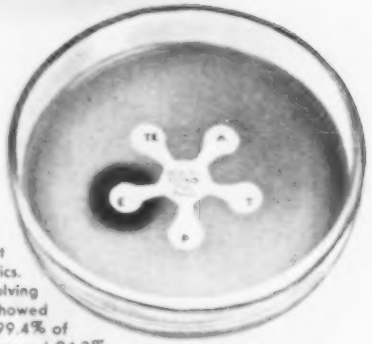
Initial dosage, one-half tablet q. i. d. Available in bottles of 100 tablets.

More Convenient for the physician . . .
Less Burdensome for the patient

Riker LABORATORIES, INC., LOS ANGELES, CALIF

DESTROYS ENTEROCOCCI

This blood agar plate shows a strain of *beta* hemolytic enterococcus. Note extreme sensitivity of this organism to ERYTHROCIN—yet it easily resists the other antibiotics. Additional data: A study[1] involving 202 enterococcic strains showed sensitivity to erythromycin in 99.4% of *alpha* hemolytic strains and 94.3% of *beta* hemolytic strains.



specific against coccic infections

Now, you can prescribe *specific therapy* against staph-, strep-, or pneumococci by simply writing *Filmtab* ERYTHROCIN Stearate. Since this coccic group causes most bacterial respiratory infections (and since these organisms are the very ones most sensitive to ERYTHROCIN) doesn't it make good sense to prescribe *Filmtab* ERYTHROCIN when the infection is coccic?

filmtab®

Erythrocin®

(Erythromycin Stearate, Abbott)

STEARATE

SPARES INTESTINAL FLORA

This sensitivity test shows ERYTHROCIN and the same antibiotics against a typical intestinal strain of *E. coli*. Note that ERYTHROCIN and penicillin do not affect this gram-negative organism—although the other antibiotics show marked inhibitory action.

1. Eisenberg, et al., Antib. & Chemo., 3:1026-1028, Oct., 1953

with little risk of serious side effects

Since ERYTHROCIN is inactive against gram-negative organisms, it is less likely to alter intestinal flora—with an accompanying low incidence of side effects. Also, your patients seldom get the allergic reactions sometimes seen with penicillin. Or loss of accessory vitamins during ERYTHROCIN therapy. *Filmtab* ERYTHROCIN Stearate (100 and 250 mg.) is supplied in bottles of 25 and 100. Abbott

filmtab®

Erythrocin®

Erythromycin Stearate, Abbott

STEARATE

®Filmtab—Film sealed tablets; patent applied for.

Continued from page 60a

parts, apply ointment or powder at night as determined by physician. **Sup:** Ointment in one-ounce tubes; powder in two-ounce shakers.

Miltown, Wallace Laboratories, Division of Carter Products, Inc., New Brunswick, New Jersey. A new tranqualizer with muscle relaxing action. Recommended in anxiety and tension states, sleeplessness due to worry and muscle spasm. **Dose:** Determined by the physician according to the need of the patient. **Sup:** In 400 mg. tablets only, bottles of 50.

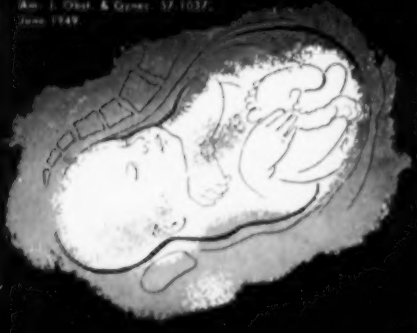
Neo-Vagisol Released with 5.0 mg. Tyrothricin, Smith-Dorsey, Div. Wander Co., Lincoln 1, Nebraska. Each Neo-Vagisol suppository contains 5.0 mg. tyrothricin. A new disposable vaginal applicator simultaneously released. **Dose:** As determined by physician. **Sup:** In boxes containing 24 suppositories and 24 disposable vaginal applicators.

Nitretamin, E. R. Squibb & Sons, Division of Olin-Mathieson Chemical Corp., New York, New York. Long-acting nitrate tablet designed to prevent attacks of angina pectoris. Contains 2 mg. triethanolamine trinitrate diphosphate. Said to be effective coronary vasodilator, not intended to substitute for quick-acting drugs, such as nitroglycerin or amyl nitrite.

Continued on page 70a

CALFERBEE

"The fetus demands and gets calcium from the mother even if her diet is deficient."
Am. J. Obst. & Gynec. 57:1037, June 1949



GIVES THE MOTHER WHAT THE FETUS TAKES

Pregnancy makes unusual nutritional demands on the mother. CALFERBEE supplies the nutriments known to be depleted by the demands of the fetus.

The gastric-resistant coated tablet not only assures better tolerance, but also assures maximum absorption of the contents for extra therapeutic effect.

Each easily-swallowed tablet provides 400 mg. *tribasic calcium phosphate*, 100 mg. *ferrous sulfate exsiccated*, the minimum daily requirement of *vitamin D*, *thiamine* and *ascorbic acid*, and ½ that of *riboflavin*.

CARROLL DUNHAM SMITH PHARMACAL COMPANY
New Brunswick, New Jersey • Established 1844

a circulatory and respiratory stimulant . . .

Coramine®

ORAL SOLUTION

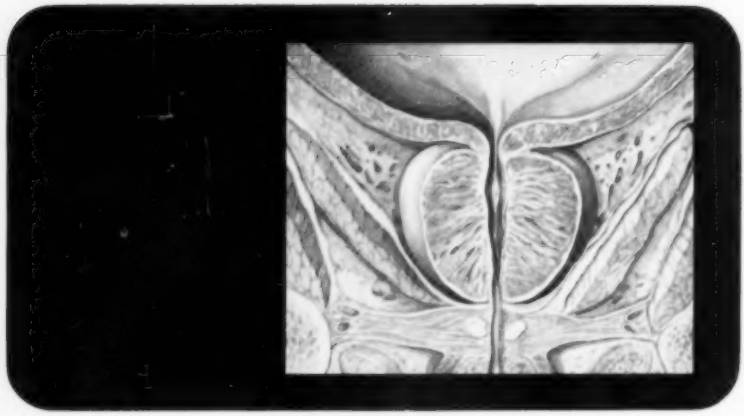
(nikethamide CIBA)

Clinical experience over many years has shown that Coramine Oral Solution is useful as a circulatory and respiratory stimulant for asthenic or elderly patients. It has been reported that Coramine Oral Solution may be beneficial in patients with coronary occlusion, in whom it appears to improve collateral circulation in the infarcted area and to stimulate the respiratory center.[1] Being noncumulative and having low toxicity, Coramine Oral Solution is suitable for prolonged treatment without danger of habituation developing. *Dosage:* ½ to 1 teaspoonful (2 to 4 ml.) 2 or 3 times a day—diluted, if desired, with water.

SUPPLIED: Coramine Oral Solution, a 25% aqueous solution of nikethamide; bottles of 1 and 3 fluid oz. and 1 pint. Also for intravenous or intramuscular use: Ampuls, 1.5 ml. and 5 ml.; multiple-dose vials, 20 ml.

1. Carey, L. S.: Delaware M. J. 21:229 (Oct.) 1949.

CIBA
SUMMIT, N. J.



acute and chronic

prostatitis...

76.6% cured or improved with

Furadantin®

brand of nitrofurantoin, Eaton

137 cases of prostatitis were treated with Furadantin with the following results:

	Acute prostatitis	Chronic prostatitis	Total
No. cases	20	117	137
Cured	15	30	45
Improved	4	56	60
Failed	1	31	32

(Personal communications to the Medical Department, Eaton Laboratories.)

Furadantin has a wide antibacterial range

Furadantin is effective against the majority of gram-positive and gram-negative urinary tract invaders, including bacteria notorious for their resistance. Furadantin is not related to the sulfonamides, penicillin or the 'mycins.

With Furadantin there is no blood dyscrasia...no proctitis...no pruritus ani... no crystalluria...no moniliasis...no staphylococcic enteritis.

Furadantin tablets—50 and 100 mg., bottles of 25 and 100. Furadantin Oral Suspension (5 mg. per cc.)—bottle of 4 fl.oz. (118 cc.).

EATON LABORATORIES

NORWICH • NEW YORK

THE **NITROFURANS**—A UNIQUE CLASS OF ANTIMICROBIALS ... PRODUCTS OF EATON RESEARCH

new product FILLS THE

THERAPEUTIC GAP IN RHEUMATIC CONDITIONS

Armyl + F

for • the patient who fails to respond to salicylates alone

• the patient who needs long-term management of residual symptoms

Each Armyl + F capsulette supplies:

Compound F (hydrocortisone-free alcohol).....2.0 mg.
Potassium Salicylate (5 gr.).....0.30 Gm.
Potassium Para-aminobenzoate (5 gr.).....0.30 Gm.
Ascorbic Acid.....50.0 mg.

Bottles of 50 capsuletles

Armyl + F is a new antirheumatic and anti-inflammatory agent with analgesic effects. It gives you significant advantages of combined simultaneous action in arthritic-rheumatic disease.

• rheumatoid arthritis and spondylitis (mild and moderately severe) • osteoarthritis (when pain is due to inflammation) • rheumatic fever (subacute phase of mild degree; subclinical relapses in children) • gout—subacute and interval gout (along with purine restriction) • bursitis, myositis, tendinitis, synovitis, fibrositis, neuritis

THE ARMOUR LABORATORIES
A DIVISION OF ARMOUR AND COMPANY • KANKAKEE, ILLINOIS

Composite X-ray visual-

in gestation

. . . nowhere will you find so much protection by such small guardians

two-a-day

GESTATABS

. . . the Mol-Iron® prenatal supplement . . . provide

- ✻ **Protection** from iron deficiency anemia with prophylactic Mol-Iron
- ✻ **Protection** from leg cramps during pregnancy with phosphorus-free calcium
- ✻ **Protection** from neonatal prothrombin deficiency with vitamin K.

The comprehensive formula of Gestatabs satisfies the nutritional demands of pregnancy—thus reducing complications, aiding delivery and improving lactation.

WHITE LABORATORIES, INC.
Kenilworth, N. J.

Vitamin A	6,000 U.S.P. Units
Vitamin D	600 U.S.P. Units
Vitamin K (Menadione)	2 mg.
Vitamin B_{12} Activity Equivalent*	2 mcg.
Folic Acid	1 mg.
Ascorbic Acid	100 mg.
Thiamine Mononitrate	3 mg.
Riboflavin	5 mg.
Pyridoxine Hydrochloride	1.5 mg.
Calcium Pantothenate	10 mg.
Nicotinamide	30 mg.
Mol-Iron	
Ferrous Sulfate	120 mg.
Molybdenum Oxide	1.8 mg.
Calcium (Elemental)**	380 mg.

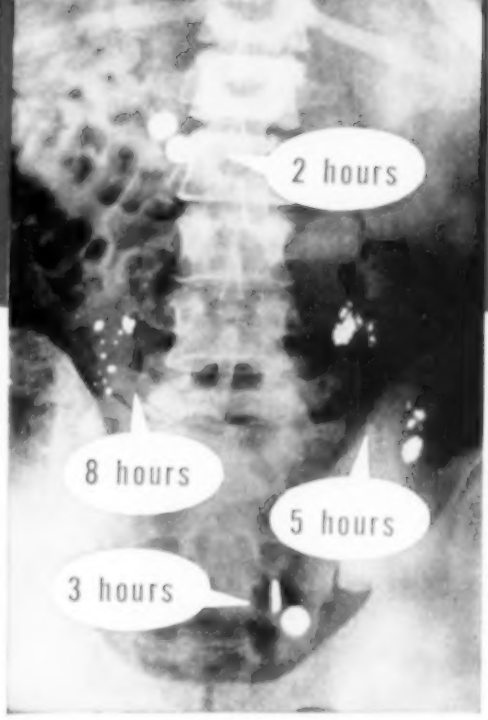
*As in Streptomyces fermentation extractives.

**Phosphorus-free from calcium gluconate and calcium carbonate.

—supplied in bottles of 60 (one month's supply) and 1000 tablets.

Also, Mol-Iron with Calcium and Vitamin D, capsule-shaped tablets—for treatment of anemia of pregnancy.

Composite X-ray visualization of the sustained release of Dura-Tab S.M. (Individual X-rays on file.)



NEW

Sustained medication with a predictable release rate

DURA-TAB S.M.*

SUSTAINED MEDICATION TABLETS†

The Wynn S.M. process is distinctive in that it provides an even, continuing release of medication over a period of 8 to 10 hours, with therapeutic effectiveness to 12 hours. The action of the medication is maintained at the optimum therapeutic level. Clinical tests over the last 2 years have proved the value of this new type of therapy.

Dura-Tab S.M. Tablets do not have a series of enteric coatings, nor are they coated granules. This new process assures a constant, predictable release of the medication, with no "up-and-down" effects.

Samples and literature on request

Dura-Tab S.M. Tablets are supplied in a number of formulas:

Homatal
Homatropine methylbromide 1/4gr.
Phenobarbital 1 gr.

Dexatal No. 1
d-Amphetamine Sulfate 15 mg.
Phenobarbital 1/4 gr.

Dexatal No. 2
d-Amphetamine Sulfate 10 mg.
Phenobarbital 1/2 gr.

Dextro-Amphetamine Sulfate
in 15 mg. and 10 mg. Dura-Tab S.M. Tablets

Wynn Pharmacal Corporation

5111-25 West Stiles Street, Philadelphia 31, Pa.

*T.M. Reg †Pat. applied for.

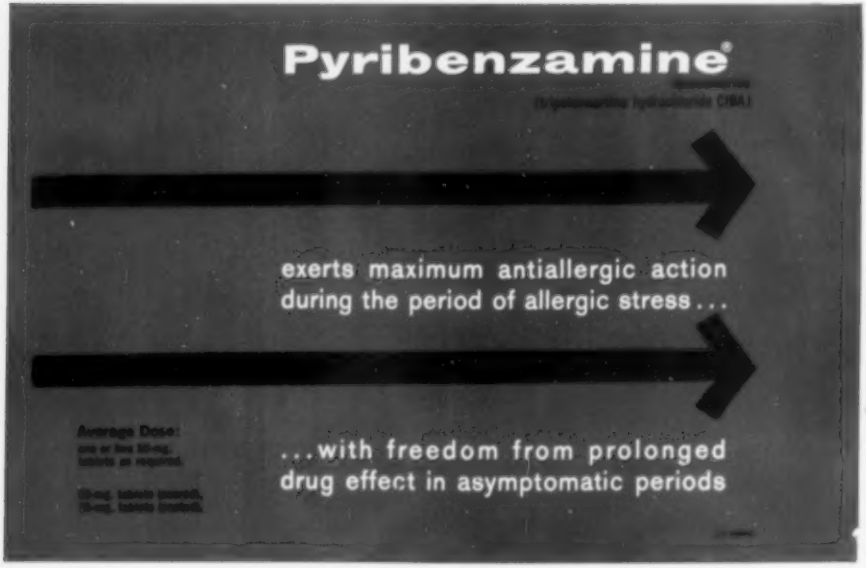
—Continued from page 66a

Full week may be required for full effect to develop. **Dose:** As determined by physician. **Sup:** In bottles of 50 tablets.

Perin, Syrup of, Endo Products, Inc., Richmond Hill 18, New York. Each teaspoonful (5 cc.) contains the equivalent of Piperazine Hexahydrate 500 mg. For pinworms and round worms. **Dose:** For pinworms—children 15-30 lbs., 1/2 teaspoonful twice daily; 30-60 lbs., 1 teaspoonful twice daily; 60 lbs. and over and adults, 2 teaspoonfuls twice daily. For round worms—children up to 60 lbs., a single dose of 1 teaspoonful for each 10 lbs. of body weight; 80 lb. and above and adults, a single dose of 2 tablespoonfuls. **Sup:** In 4 fl. oz., and pints.

Placidyl, Abbott Laboratories, North Chicago, Illinois. A mild, nonbarbiturate hypnotic. Offers a gentle source of sleep for patients troubled by ordinary nervous insomnia. Provides mild hypnosis without initial excitation or hangover. Takes effect within 15 to 30 minutes and sleep should last all night. **Dose:** Recommended adult dose for pleasant induction of sleep is 500 mg. at bedtime. **Sup:** In 500 mg. capsules, bottles of 100.

Prelafal, Ayerst Laboratories, New York 16, N. Y. A new dietary supplement providing essential vitamins as well as phosphorus-free calcium, aluminum hydroxide gel, and vitamin K. **Dose:** As determined by physician. **Sup:** In 100's and 500's tablets.



Solu-Cortef Injection, The Upjohn Company, Kalamazoo 99, Michigan. Hydrocortisone therapy for intravenous use: particularly suitable in emergency situations where immediate high levels of circulating hydrocortisone are required. **Dose:** As determined by physician. **Sup:** In 100 mg. vials.

Sulfa-Plex, Rowell Laboratories, Baudette, Minnesota. A balanced concentration of four sulfonamides—total content of 10%. A vaginal cream for treatment of non-specific vaginitis, cervicitis, ulcerative vaginitis and postoperative conditions of the vagina and cervix. **Dose:** As indicated by physician. **Sup:** In two-ounce tubes with and without applicator.

Sulfid, The Columbus Pharmacal Co., Columbus, Ohio. Brown, coated tablet containing phenylazo-diamino-pyridine HCl 50 mg. and sulfacetamide 250 mg. For treatment of urinary tract infections. **Dose:** Administered according to directions of physician. **Sup:** In bottles of 100 and 1,000 tablets.

Tricofuron Suppositories and Powder, Eaton Laboratories, Norwich, New York. Tricofuron vaginal suppositories contain Furoxone, brand of furazolidone 0.25% in a water-miscible base composed of Carbowax and 20 dendro palmitic acid. The powder contains Furozone 0.1% in a water-soluble powder base composed of lactose, dextrose and citric acid. Both suppositories and powder are used concomitantly for trichomonas vaginalis vaginitis and the accompanying secondary bacterial infections. **Dose:** Suppositories: first week, one suppository in morning and one at bedtime. After first week, one suppository at night. Powder: Insufflation by physician of the entire vaginal vault and cervix 2 times

—Concluded on page 74a

—Continued from page 73a

weekly. **Sup:** Suppositories of 2 Gm., box of 12. Powder in 30 Gm. bottle.

Tylenol, McNeil Laboratories, Philadelphia, Pennsylvania. Red-colored elixir containing 120 mg. N-acetyl-p-aminophenol per 5 cc. For reduction of fever and relief of discomfort. Analgesic-antipyretic preparation designed for treatment of infants and young children. Product used alone or in combination with other drugs, such as antibiotics and sulfonamides. **Dose:** As determined by physician. **Sup:** In bottles containing 4 fl. oz. and 12 fl. oz.

Viflavia, Columbus Pharmacal Company, Columbus 15, Ohio. Contains citrus bioflavonoid, 100 mg., ascorbic acid, 100 mg., menadione 0.5 mg. For the maintenance of normal capillary strength and permeability. **Dose:** Therapeutic — 2 capsules 4 times daily one week; maintenance and prophylactic — 1 capsule q.i.d. **Sup:** In bottles of 100 and 500 capsules.

Vinufer Liquid, Carroll Dunham Smith Pharmacal Co., New Brunswick, New Jersey. Each 5 cc. contains ferrous gluconate 100 mg., vitamin B_{12}, 10 mcgm., thiamine hydrochloride 2 mgm., pyridoxine hydrochloride 2 mgm., alcohol 5% and aromatics. The well-rounded liquid hematinic. **Dose:** Suggested dosage for adults is 2 teaspoonfuls three times daily. **Sup:** In pints.

IN ANXIETY AND TENSION

Sedation without hypnosis

IN HYPERTENSION

a safer tranquilizer and antihypertensive

"It's just mumps, but stay away from Texas next time."

FOR MAINTENANCE THERAPY

℞ as little as
0.1 mg. per day

Serpasil

(reserpine CIBA)

a pure crystalline alkaloid of rauwolfia root first identified, purified and introduced by CIBA

CIBA SUMMIT, N. J.

NUTRITIONAL AND THERAPEUTIC ADJUVANTS IN HEALTH AND DISEASE

Bioflavonoids of Orange and Lemon

Hesperidin Complex
Lemon Bioflavonoid Complex
Hesperidin Methyl Chalcone
Calcium Flavonate Glycoside

Action of the bioflavonoids on the capillary

Maintenance of normal capillary integrity
For the treatment of abnormal capillaries such as:
Increased fragility
Increased permeability
Decreased resistance

Bioflavonoid activities in cellular metabolic processes

Hyaluronidase inhibition
Antihistamine effect
Closely related to the activity of the adrenal cortex
Inhibition of epinephrine oxidation
Sparing action on vitamin C
Synergism with vitamin C

Indications

As adjuvants in many disease states having capillary impairment including:
Habitual abortion
Respiratory diseases
Inflammatory diseases
Vascular diseases
Geriatrics

Exchange Brand Bioflavonoids are available to the medical profession in pharmaceutical specialties through leading pharmaceutical manufacturers.

Sunkist Growers
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Exchange

PHARMACEUTICAL SALES • ONTARIO, CALIFORNIA

a Brighter Prognosis for your

HERPES ZOSTER PATIENTS

when you use

PROTAMIDE®

(Sherman)

because published studies* show:

"Good to excellent results" in more than 80%, with "almost immediate improvement."

Prompt recovery in more than 90% when Protamide is started in the first week of symptoms.

Why not use Protamide first?

. . . for herpes zoster, post-infection neuritis, chickenpox, and other nerve root pain such as tabes dorsalis.

A sterile colloidal solution prepared from animal gastric mucosa . . . denatured to eliminate protein reaction . . . completely safe and virtually painless by intramuscular injection.

CLINICAL DATA ON REQUEST

*Combes, F. C. & Canizares, O.: New York St. J. Med. 52:706, 1952; Marsh, W. C.: U. S. Armed Forces M. J. 1:1045, 1950.

SHERMAN LABORATORIES

WINDSOR • DETROIT 16, MICHIGAN • LOS ANGELES

offering prompt relief

DUAL-ACTION

Terra-Cortril*

TOPICAL OINTMENT

provides a gratifying response in a wide range of dermatoses, quickly resolving inflammation, as well as eradicating primary or secondary pyogenic infection.[1]

supplied: in 1/2-oz. tubes, containing 3% oxytetracycline hydrochloride (TERRAMYCIN®) and 1% hydrocortisone, free alcohol (CORTRIL®) in an easily applied ointment base.

Cortril Topical Ointment
Cortril Tablets
Cortril Acetate Ophthalmic Ointment
Cortril Acetate Aqueous Suspension for intra-articular injection
Terra-Cortril Ophthalmic Suspension

Pfizer

PFIZER LABORATORIES
Division, Chas. Pfizer & Co., Inc.
Brooklyn 6, New York

*brand of oxytetracycline and hydrocortisone
†Trademark

1. Robinson, H. M., Jr., et al.: South. M. J. 46:773, 1953.

"Please Mr. Scott, this conference is for us doctors only . . . if you please!"

METICORTEN

PREDNISONE (metacortandracin)

Schering

more potent than cortisone
or hydrocortisone · devoid of
major undesirable side effects

T.M. METICORTEN, brand of prednisone

the Resions

...specifics in diarrhea

The RESIONS offer two effective compounds for treatment of almost any diarrheal condition found in clinical practice.

The RESIONS act by ion exchange . . . to attract, bind and remove toxic materials in diarrheas caused by food or bacterial toxins, by prolonged use of certain drugs, and in general infectious diseases.

The RESIONS *are safe* because they are totally insoluble and non-toxic.

RESION therapy will control about 90% of common diarrheas.

RESION P-M-S is intended specifically for rapid control of those rare diarrheas caused by Gram-negative organisms; to prevent secondary bacterial infection; in mycotic diarrhea following the use of the broad-spectrum antibiotics, and to inhibit the enteric growth of *C. albicans* (Monilia).

Resion

time-tested, adsorbent effectiveness

Polyamine methylene resin	10%
Sodium aluminum silicate	10%
Magnesium aluminum silicate	1.25%

CONGO MAGIC
(Dysentery Fetish)
Resion therapy now works scientific magic against diarrhea.

and

Resion P-M-S

A new formula providing antibacterials to combat bacillary and fungal vectors

Each 15 cc. contains the RESION formula plus:

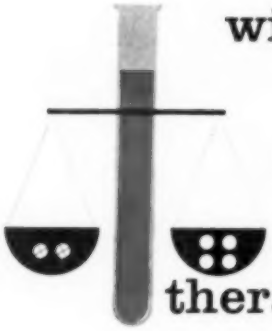
Polymyxin B sulfate	125,000 units
Phthalylsulfacetamide	1.0 Gm.
Para hydroxybenzoic acid esters	0.235 Gm.

Dosage: RESION—1 tablespoonful hourly for 4 doses; then every 3 hours while awake. RESION P-M-S—1 tablespoonful hourly for 3 doses; then 3 times daily.

Supplied: RESION, in bottles of 4 and 12 fluid ounces. RESION P-M-S, bottles of 4 fl. oz.

THE NATIONAL DRUG COMPANY
Philadelphia 44, Pa.

". . . Fornasan complicated with a little crintz, nothing really serious, but we must be sure it doesn't develop into kanafan, absolutely no candy, cake and malteds for a week or we may have to anaferon with the brivin . . ."



with half the dosage* –equal therapeutic effect

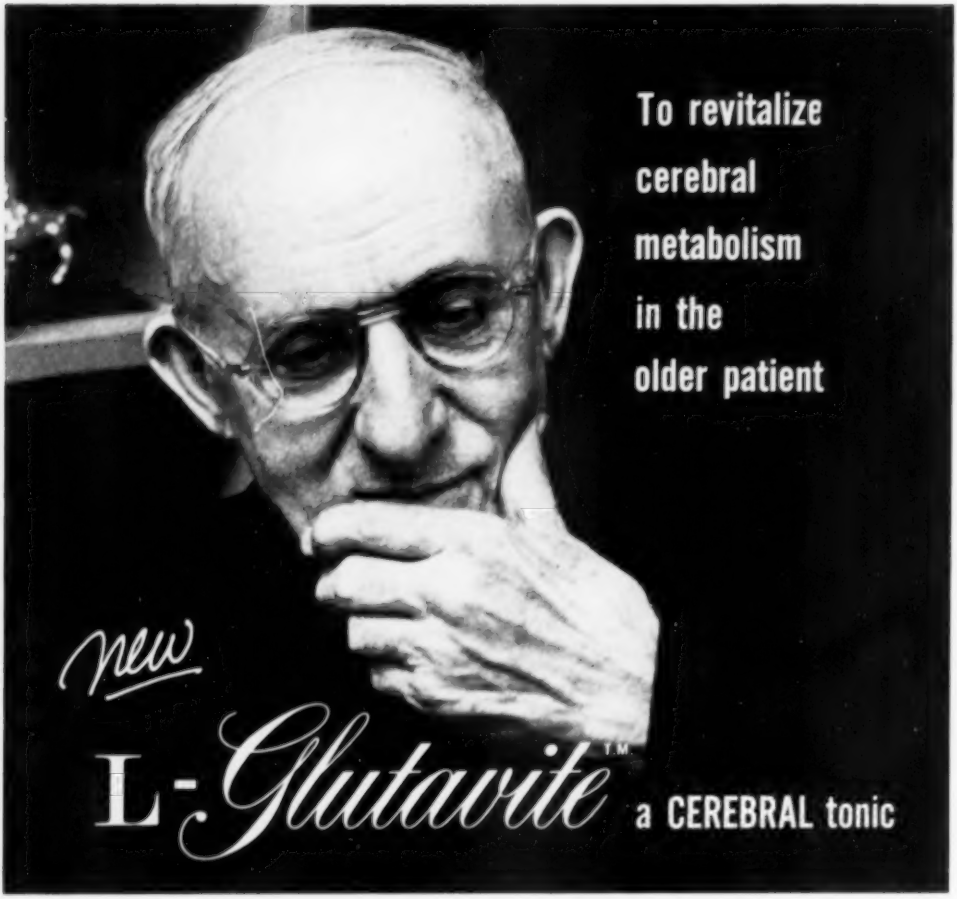
CIBA
SUMMIT, N. J.

*Elkosin maintains effective blood levels, both in urinary and systemic infections, with standard (i.e., sulfadiazine) dosage, or approximately *half* the dosage required with the other widely used sugar-soluble sulfonamide. This means extra safety, and greater convenience and economy.

ELKOSIN®

SAFE, SOLUBLE, BROAD SPECTRUM SULFONAMIDE

TABLETS	SUSPENSION IN SYRUP
0.5 Gm. (White, double scored)	0.25 Gm. per 4 ml. teaspoonful



L-Glutavite is specifically formulated to assist in the treatment of geriatric patients whose symptoms of weakness, apathy and fatigue are characteristic of waning cerebral metabolism. Himwich[1] reports excellent results with sodium glutamate in such cases, while Lehmann states that "a trial with nicotinic acid is always indicated . . ."[2] By combining these key factors with other vital nutritional elements, L-Glutavite effectively increases cerebral blood flow while it enhances the ability of cerebral tissue to utilize the increased nutrients provided. This unique therapeutic formula helps the tired, the apathetic, the depressed individual to face life more actively, and with greater interest.

Supplied in cartons of 30 individual dosage packets; initial dose, 3-5 packets per day for 5 to 6 weeks. Pleasant-tasting appetite-stimulating powder, to be mixed in fruit juices or sprinkled on food. Contains monosodium L-glutamate, niacin, thiamine, riboflavin, ascorbic acid, ferrous sulfate and dicalcium phosphate, in high potencies.

1. Himwich, H. E.: Paper presented at American Psychiatric Association meeting, St. Louis, May, 1954.
2. Lehmann, H.: 22nd Annual Conference, Mirbane Memorial Fund, New York, Paul B. Hoeber, Inc., 1952, p. 587.

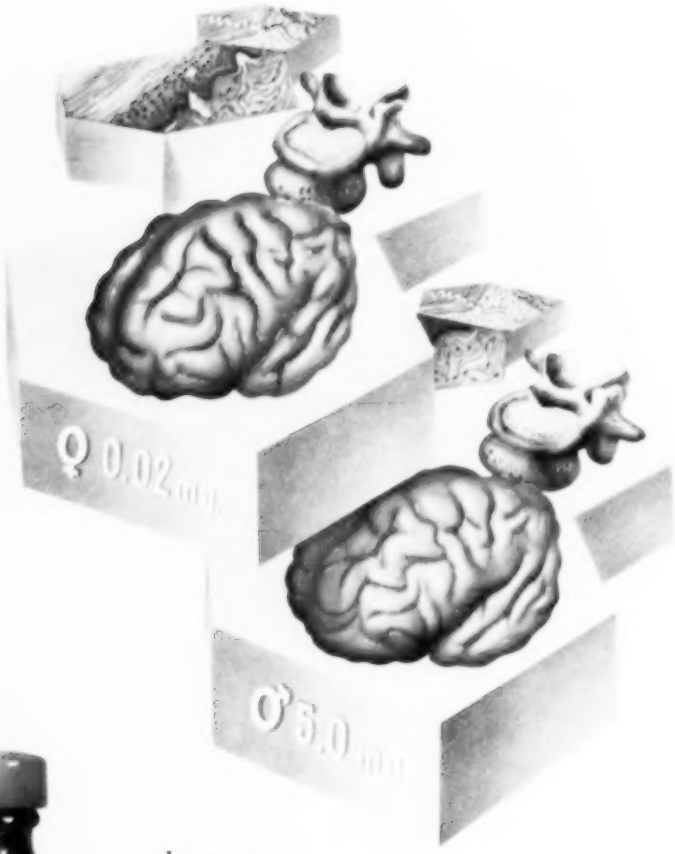
GRAY PHARMACEUTICAL CO., INC., Newton 58, Massachusetts

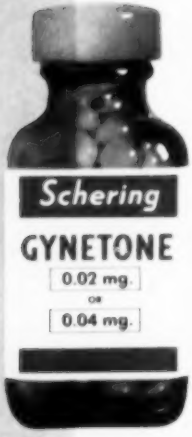
for the upset

menopausal woman . . .

real relief

GYNETONE® androgen-estrogen therapy
REPETABS® 0.02 and 0.04, and by injection.





because

the tonic effect

of estrogen-androgen

revitalizes tissues

relieves refractory symptoms

restores composure and sense of well-being

contains 0.02 mg. ethinyl estradiol
plus 5 mg. Methyltestosterone

also available with 0.04 mg. ethinyl estradiol
plus 10 mg. Methyltestosterone

Syrup and oral tablets. Each teaspoonful or tablet of HYCODAN contains 5 mg. dihydrocodeinone bitartrate and 1.5 mg. Mesopin.* May be habit-forming. Average adult dose, 1 teaspoonful or 1 tablet after meals and at bedtime.

Hycodan®

(Dihydrocodeinone with Homatropine Methylbromide)

BETTER THAN CODEINE **FOR COUGH**[1]

FASTER • LONGER-LASTING • MORE THOROUGH

BETTER THAN CODEINE *PLUS* APC **FOR PAIN**[2]

Percodan®

(Salts of Dihydrohydroxycodeinone and Homatropine, plus APC)

Scored, yellow oral tablets. May be habit-forming. Average adult dose, 1 tablet q. 6 h.

1. Hyman, S., and Rosenblum, S. H.: Illinois M. J. 104:257, 1953.
2. Piper, C. E., and Nicklas, F. W.: Industr. Med. 23:510, 1954.

U. S. Pat. 2,628,185

your best bet!

Literature? write

ENDO PRODUCTS INC., RICHMOND HILL 18, NEW YORK

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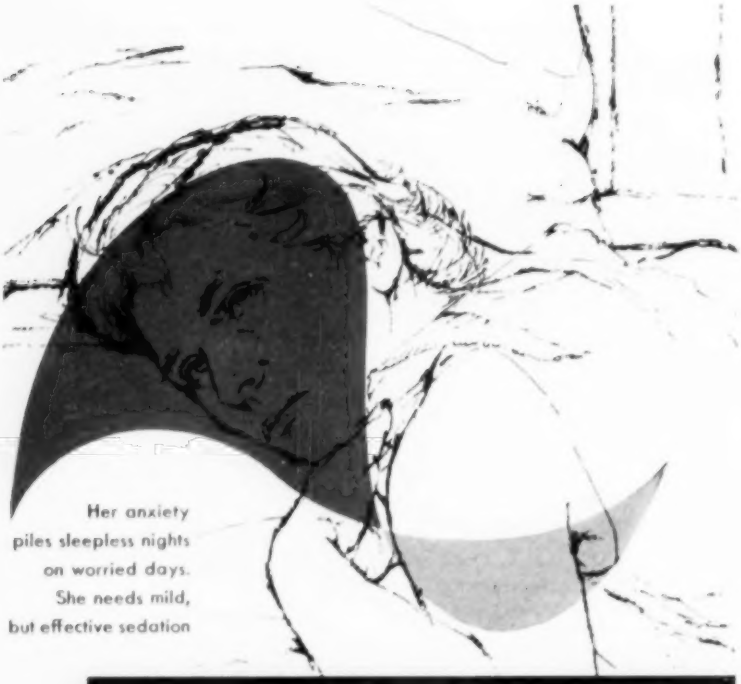

for a sound sleep tonight, a calm day tomorrow . . .

filmtab

Nembu-Serpin

Just one tablet at bedtime of this new combination of NEMBUTAL and Reserpine will calm the worries of most patients with mild anxiety states. Yet, patients have a sense of well-being the next day—keep their drive and energy. The synergistic effect of the combination produces smooth, gentle, prolonged sedation: NEMBUTAL acts quickly to induce drowsiness at bedtime, Reserpine sedation calms the patient through the following day. Small dosage makes side effects rare. Also recommended for treatment of mild essential hypertension. Prescribe NEMBU-SERPIN to give your anxiety patients a sound sleep tonight, a calm day tomorrow. In bottles of 100.

Abbott

Each NEMBU-SERPIN Filmtab contains—NEMBUTAL* Calcium (Pentobarbital Calcium, Abbott), 30 mg. ($\frac{1}{2}$ gr.) and Reserpine, 0.25 mg.

*Filmtab—Film-sealed tablets, pat. applied for.

Rheumatoid Arthritis

Evaluation of an Embryonic Bone Marrow Malic Acid* Preparation in Its Treatment — A Preliminary Report

LAWRENCE W. SMITH, M.D.
New York, New York

Experimental injections of aqueous, deproteinized and defatted extracts of liver, spleen, thymus, lymph gland and red bone marrow in animals are accompanied by transient but consistent lowering of blood pressure. If the injections are made into animals that have been bled to produce anemia, the blood pressure changes occur together with varying but definite response in the red cell count and in hemoglobin.[1,2]

Chronic disease, especially rheumatoid arthritis, is often attended by some hypertension and more especially by hypochromic anemia. These various extracts have been investigated in an attempt to value the relative effectiveness, if any, on the hypochromic anemia that occurs in rheumatoid arthritis. In the course of these studies a favorable recovery of the red cell count was observed, and a somewhat unexpected and outstanding clinical response occurred, with cessation of pain, improvement in the mobility of stiffened joints and a significant over-all feeling of well-being. Urinary changes included a marked phosphaturia and according to one investigator, ketosteroid substances were eliminated in substantial amounts.[3]

The tissue extracts were not equally effective. As nearly as could be evaluated, red bone marrow excelled greatly over liver and spleen and these in turn appeared to be more active than thymus or lymph node extracts. A considerable bibliography regarding the therapeutic use of various organic acids such as ascorbic, lactic and malic, exists especially in the older literature. The basis for its reported clinical effectiveness appears to be dependent upon its action on certain enzyme systems. In some early studies malic acid alone was employed in treating patients with arthritis and other painful conditions with some slight though inconsistent measure of response. However, when highly purified malic acid was added to the tissue extracts, the combined activity was greater than the individual action of either, and the combination that yielded uniformly maximum therapeutic value consisted of

* Carbartrol®, Carbon Research Corp., of New York.

embryonic bone marrow (calf) and malic acid. This particular combination has been designated Cerbartrol and was made available to me for clinical appraisal in the treatment of rheumatoid arthritis.

Embryologists recognize the genetic relationship that the tissues mentioned bear to the physiological evolution of hematopoiesis, a function that begins extra-embryonically in the yolk sac and is successively transferred to the embryo's liver, spleen, thymus and lymph nodes; at birth and thereafter to the red bone marrow. Gradually the red bone marrow retrenches, and by adolescence it is largely displaced by hematopoietically inert yellow bone marrow. It is interesting, but perhaps only speculative, that the age of rheumatoid arthritis onset correlates with the displacement of red bone marrow. It is well known that rheumatoid arthritis shows "spontaneous" phases of clinical remission and relapse and this characteristic must be kept in mind when any new treatment undergoes assessment.

When a new treatment is proposed for any refractory clinical entity such as rheumatoid arthritis, it is quite usual for the investigator to find immediately available only such cases as have failed to respond appreciably, if at all, to previous standard forms of therapy. This common tendency is statistically justifiable if it is looked upon as stratified randomization. When I obtained Cerbartrol for study there were seventeen cases of rheumatoid arthritis available to me all of which had previously received cortisone with unsatisfactory response. For one reason or another, cortisone therapy in this group had to be discontinued, either because of intolerable side reactions or because of failure to improve. There were in this group, therefore, 0 cortisone success and 17 cortisone failures.

All were put on a "course" of Cerbartrol injections. Each millilliter of Cerbartrol represented the extract from 10 grams of embryonic bone marrow (calf) and 8 milligrams of malic acid combined by a special process. The instruction was to inject 0.3 to 0.4 milliliters daily. Larger doses are apparently without corresponding greater effectiveness. The principal admonition is perserverance until at least 30 to 40 daily or alternate day injections have been administered. Thereafter, the injections are furnished as needed, perhaps once or twice a week.

Unlike cortisone, the objective response to Cerbartrol is not usually immediate. Several days are usually required before pain subsides and in some instances two or three weeks of Cerbartrol medication is needed to bring satisfying relief. The appetite improves, most often there is a gain in weight, restful sleep is experienced and in some individuals irregular bowel habits are regulated.

Swollen joints are reduced and mobility is increased. Hypochromic anemia is corrected. Mild hypertension is sometimes lowered. The sedimentation rate, frequently above normal, returns toward normal. In a few individuals an eosinopenia was noted, but no other change in the differential white cell count occurred.

Of the 17 patients, 13 responded as indicated and were outstandingly improved objectively and subjectively. 4 cases rallied temporarily but not sufficiently to consider that they had benefited substantially from the injections.

The problem is to evaluate the statistical significance of the 13 successes and 4

failures in the same group that previously had furnished no successes and 17 failures on cortisone treatment. An adequately appropriate statistical test is chi-squares with Yates correction[4] as follows:

TABLE 1

TREATMENT	SUCCESSES	FAILURES	TOTAL
Cortisone	0	17	17
Cerbartrol	13	4	17
TOTAL	13	21	34

Calculation with these data gives a chi-square value of 17.93 (with Yates correction) which is very highly significant, there being considerably less than one in a thousand probability that the difference between the two treatments is due solely to chance.

Selection of the chi-square statistic for comparative evaluation of the cortisone and Cerbartrol treatments was purposeful because it could be used again in comparing my results with the reports of several Italian clinicians.[5,6,7] Of 15 cases of rheumatoid arthritis the Italian physicians reported 12 successes and 3 failures. These received only Cerbartrol and were not residual cases left over from cortisone failure. Here is a comparison:

TABLE 2

EXPERIMENTER	SUCCESSES	FAILURES	TOTALS
Smith	13	4	17
Italian	12	3	15
TOTAL	25	7	32

Again on calculation, chi-square gives the value 0.0393. This is a very close agreement and indicates that the difference in the result gives no proof of more than chance variations (probability greater than 90 percent).

It is probably generally conceded that cortisone type of hormones have a limited place, if any, in the management of osteoarthritis as opposed to rheumatoid arthritis. It was not difficult to assemble 18 osteoarthritics who routinely failed to respond to cortisone treatment. This same group, however, treated with Cerbartrol gave 14 unmistakably positive responses, subjectively and objectively, 2 indifferent responses and 2 negative responses.

TABLE 3

ENUMERATION OF RESPONSE OF OSTEOARTHRITICS TO CORTISONE AND CERBARTROL

	IMPROVED	UNIMPROVED	TOTAL
Cortisone	0	18	18
Cerbartrol	14	4	18
	14	22	36

For these findings the value of chi-square (with Yates correction) is 27.35. —a very highly significant figure. Statistically the probability is considerably less than 1 in 1,000 that the difference between the two treatments can be ascribed to chance alone.

A striking difference in the biochemical reactivity of Cerbartrol as contrasted with cortisone is therefore revealed in Cerbartrol's ability satisfactorily to improve subjective and objective symptomatology in osteoarthritis as in rheumatoid arthritis; and since the enumeration in each group of cases was arrived at by ascertaining the chi-square value it is permissible to cast the following table for further comparison.

TABLE 4

RESPONSE TO CERBARTROL BY OSTEO-ARTHRITICS AND RHEUMATOID ARTHRITICS

	IMPROVED	UNIMPROVED	TOTAL
Osteo-arthritics	14	4	18
Rheumatoid arthritics	13	4	17
	27	8	35

These data, with Yates correction applied, give a chi-square value of 0.147. Since chi-square values of 3.841 are considered not significant at the 5% level of confidence it is obviously clear that for all practical purposes Cerbartrol is as clinically effective in osteo-arthritis as it is in rheumatoid arthritis. In distinction cortisone is not especially indicated in osteoarthritis and in those cases of rheumatoid arthritis wherein cortisone failed to give relief, or needed to be discontinued for whatever reason, Cerbartrol effected unmistakably significant improvement.

Summary

Embryonic bone marrow, defatted, deproteinized and supplemented with Malic Acid in rheumatoid arthritis gave highly significant statistical evidence of effectiveness in cases that had failed to respond to cortisone.

The results obtained in a series of 17 cases completely corroborated the findings in 15 cases reported on by Italian physicians using the same treatment.

Similarly the 18 cases of Osteo-arthritis that had previously been treated unsuccessfully by hormone therapy responded to Cerbartrol treatment with the same statistically significant results.

In the face of such significant statistical evaluation, it seems proper to recommend the use of Cerbartrol in treatment of rheumatoid-osteo-arthritis.

Bibliography

1. Brown and Guthrie, Am. J. Physiol.—14: 328-1905.

2. Brown and Joseph, Am. J. Physiol.—16: 110-1906.

3. Rheumatological Center of Rome, Dr. Prof. T. Lucherini & Dr. Gustavo Tuccimei—MINERVA MEDICA ANNO XLII, Vol. II—No. 60—Sept. 15, 1951.

4. Dixon and Massey, Introduction to Statistical Analysis—McGraw Hill—New York 1951.

5. United Institute of Assistance & Beneficence of the City of Rome, Dr. A. Curatolo & Dr. F. M. Cerbini on the GAZZETTA INTERNAZIONALE of Medicine & Surgery—ANNO LIV No. 12—December 1950 [629-731].

6. Instituto di Clinica Medica Generale della Universita di Pavia, Director Prof. P. Introzzi—Rivista "IL SANGUE" No. 5—1951—by B. Rovatti, M.D.

7. Scorpati G. "Clinical Observations on The Action of A Preparation Based On Malic Acid Associated With A Fraction of Bone Marrow"—GAZZETTA MEDICA ITALIANA CXIII—No. 7—July, 1954—Sanatorio Ramazzini Bernardini.

8. Centro di Reumatologia di Roma, Director Prof. T. Lucherini — "Terapia delle Malattie Reumatiche Con Estratto di Midollo Osseo"—"GAZZETTA INTERNAZIONALE DI MEDICINA E CHIRURGIA"—Anno LIX, Vol. LX, 1955—by Dr. Sergio Venanzi.

9. Sonderdruck aus Heft 11/12.7. Jahrgang (1952), der Zeitschrift "DER KREBSARZT"—"Ergebnisse der Krebsbehandlung mit einem Knochenmarkspraparat"—by Bernardini Rovatti, M.D. and Giuseppe Gasparini, M.D., New York.

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Sexual Impotence

Because of the intensity of the biological needs and drives in Man "to multiply upon the face of the earth", he has been intensely and anxiously concerned with his virility and potency to engage in coitus. Possibilities of impotence have plagued him from time immemorial, even in his sleep!

Definition[20] Impotentia is the condition where there is an inability to perform normal sexual intercourse, encompassing all manifestations of sexual insufficiency whether because of lack of desire, inability to have or maintain erection, faulty or absent ejaculation, non-erectile, painful, or premature ejaculations or actual physical defect precluding technical possibilities of satisfactory coitus—which may be partial or complete, temporary or permanent.

Historical While study and attempted cures of impotence have preoccupied medicine men, soothsayers, witch-doctors, trance-mediums, astrologers, alchemists, quacks and honest medical researchers down through the years it was not until recent times that medical men thought they were approaching the answer. The "Birthday of Endocrinology"[2] was thought to have occurred on the 1st of June, 1889. It was on this date that Brown-Séquard reported to the Société de Biologie de Paris on the use of testicular extract on himself at the age of seventy-two—and supposedly successfully!

There were many disappointing and conflicting reports that followed in the wake of his exploratory endocrine attempts.

In 1929, the isolation of androsterone from the urine of young men was accomplished by French and Harrow. This was furthered by an extract five to ten times as potent from testicular tissue by Koch and Gallagher. Finally, in 1935, Laquer et al. isolated testosterone.

Immediately, hopes rose.

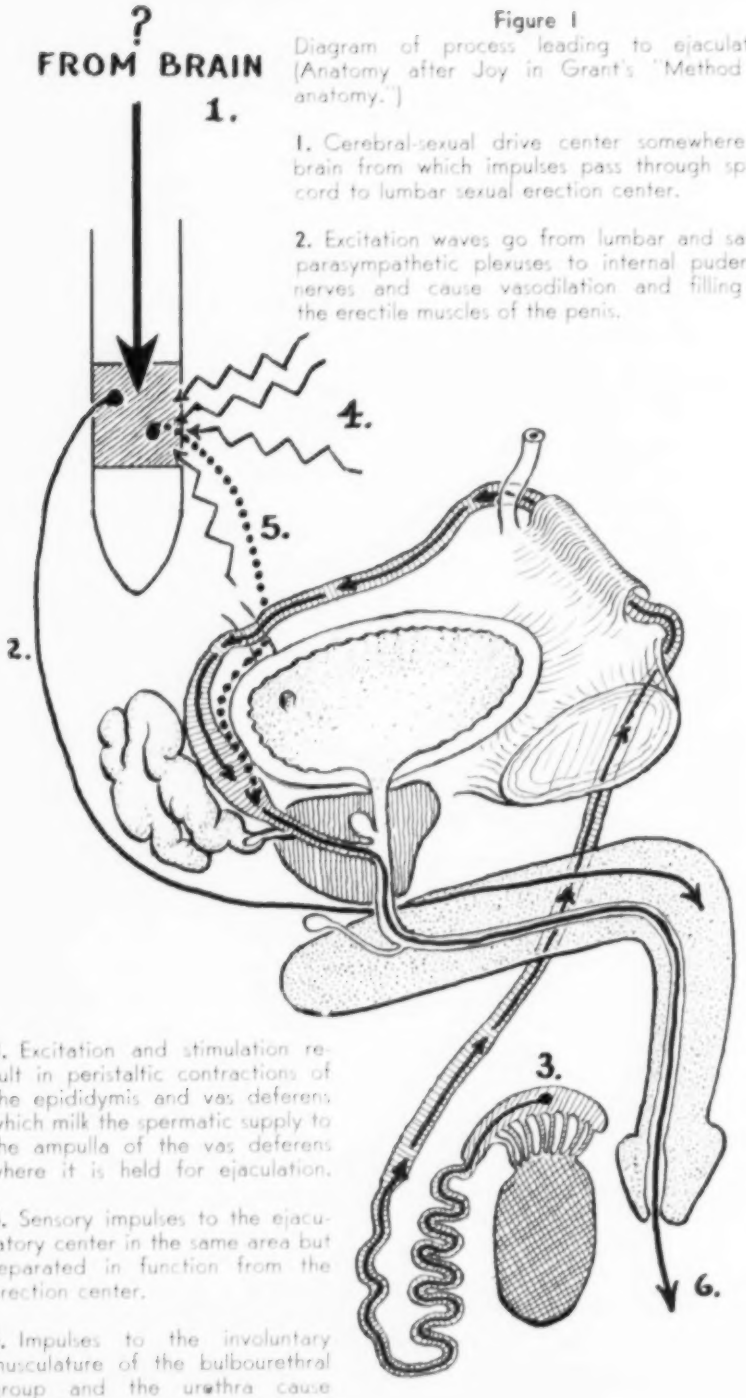
However, here again, exact and measured interpretations of results achieved by responsible investigators became well-nigh impossible because of personality problems and life-situations involved in all their diverse complexities. Today, proper evaluation without adequate control cases still makes the problem difficult to settle.

Physiology[1, 20, 21, 37, 39] It is felt that there is a cerebral sexual-drive center although its location in the brain is not known. However, to this center comes the complex of desire from the senses and the imagination. From it go the impulses through the spinal cord to the lumbar sexual erection center.

The nervi erigentes then carry the excitation waves through the lumbar and sacral parasympathetic plexuses to

Figure 1

Diagram of process leading to ejaculation (Anatomy after Joy in Grant's "Method of anatomy.")



1. Cerebral-sexual drive center somewhere in brain from which impulses pass through spinal cord to lumbar sexual erection center.

2. Excitation waves go from lumbar and sacral parasympathetic plexuses to internal pudendal nerves and cause vasodilation and filling of the erectile muscles of the penis.

3. Excitation and stimulation result in peristaltic contractions of the epididymis and vas deferens which milk the spermatic supply to the ampulla of the vas deferens where it is held for ejaculation.

4. Sensory impulses to the ejaculatory center in the same area but separated in function from the erection center.

5. Impulses to the involuntary musculature of the bulbourethral group and the urethra cause ejaculation.

the internal pudendal nerves affecting the blood supply of the corpora cavernosa and corpus spongiosum of the penis. Vasodilation and filling of the erectile muscles result.

With further excitation and stimulation peristaltic contractions of the epididymis and vas deferens occur. This milks a spermatic supply to the ampulla of the vas deferens and it is there held for the ejaculation.

Sensory impulses, increasing in intensity, are returned to the ejaculatory center in the spinal cord, in the same area, but separated in function from the erection center. High-intensity, intermittent impulses are transmitted to the involuntary musculature of the urethra and to the voluntary musculature of the bulbourethral group. Ejaculation then occurs.

The final stimulus may be furthered or inhibited from the brain or from the peripheral nerve endings.

The Endocrine Glands play important and complex roles in the establishment and maintenance of potency. In order of descending importance they are the testicles, pituitary, adrenals, thyroid, pancreas, and thymus. It is believed that the prostate gland plays little if any role in potency.[18]

This impressive study[18] contradicts the work of another writer[2] on the possible role of prostatic pathology in furthering impotentia. Rose and Kimbrough, in their series of prostatectomies, state that if there was no power prior to operation there was little chance of its return afterwards. If there was power prior to operation then there was a 50% chance of its return afterwards. 63% claimed decrease in general sex activity. 3.1% claimed an increase.

The role that Vitamin E may play in potency has only been adequately investigated in lower animals.

Contributory Factors Most writers today feel that derangement of sexual function has its commonest background 85-95%[2, 5, 12, 27, etc.] in psychopathology of one type or other. The organic factors are a minor group.

Be that as it may, it is simpler for us to consider the anatomic and physiologic possibilities first of all. Actually, while the sum total of them constitute together a small minority of the causes of Impotentia in the male medical practice has busied itself with them because they were simpler to find and to treat.

Sexual union failures include (1) accidental deprivation of the genitals (2) physical size incompatibility of partners (3) a physiologic group, such as childhood, senility, and post-coital period (4) a somatogenic group, such as malformation of the penis, urologic pathology, malnutrition, vitamin deficiencies, certain central-nervous-system diseases, constitutional disorders, fatigue, etc., (5) endocrine dyscrasias, principally hypogonadism as it appears in castrates, male climacteric, old age.

While the proper psychoanalytical weightings are difficult to evaluate where the various organic factors mentioned above are lacking or minimal, it must be remembered that most workers in the field today state that the psychogenic disabilities form the vast majority. They include various types of inhibitions, worries, repressions, apprehensions and unrelieved, unresolved memorable anxieties.

It is also wise to keep in mind even where there are minor somatic disorders present that the psychic overlay may have become the overwhelming

burden in impotentia! Here, Croley[6] with his "Secrets of India" may have been of more temporary help than the family doctor who spoke vaguely and alarmingly to his patient about its "just being your nerves". How much better the therapeutic assurance of the knowledgable physician!

No attempt will be made here to minimize the importances of structure, accident, disease: infectious or infestating, or the effects of various debilities or toxins. Problems with partners have been recently pointed out in an admirable paper by Hulse.[7] Another writer[8] puts it as follows: "Male potency is highly susceptible to psychic and physical changes in his partner . . . requires investigation." He cites many cases to prove this point.

Impotence from the use of certain antihistamines has been allegedly demonstrated.[9] A syndrome has been described[11] of anhidrosis, orthostatic hypotension and impotence and related to a CNS dyscrasia. Yet others[13] have detailed injuries to the cord between the 6th thoracic and the 3rd lumbar or the cauda equina roots without interfering with potency or fertility! Segaloff[12] has even shown that many testicular dysfunctions do not appear to be related to potency. And Hemphill[18] vigorously points out that many cases of obsessional neuroses with impotence have returned to normal gonadism and sexual behavior after prefrontal leucotomy.

Defects of Structure Many of these are readily amenable to various surgical techniques. Included in this group are hypospadias, epispadias, simple tumors of the penis, phimosis, growths, fibrous bands or edema and chordee of the shaft. We can include minor traumatic defects too.

Reinforcement of the deficient or deformed erectile tissues has been accomplished successfully in selected cases in the young by cartilage transplants.[10]

The classic work in this field has been done by Lowsley[24, 25] and his workers. They now have over 18 years of experience with the operations involving the plication of the bilateral ischiocavernosus and the bulbocavernosus muscles. Their results were best in traumatisms of the urethral or perineal structures; and in changes occurring as the result of excessive sexual activity, including masturbation.

Infections Almost any chronic infection contributing to debility or systemic fatigue may be causal to loss of virility. The major ones include syphilis, diabetes, mumps, tuberculosis, the general contagious fevers, the various anemias and blood dyscrasias, and possibly, the focal infections.

Local infections of the genitourinary apparatus also add their numbers to Impotentia. Gonorrhea, tuberculosis, verumontanitis, prostatitis, polyps of the posterior urethra, posterior urethritis.

Various CNS disorders must not be overlooked. The infections include encephalitis, the meningitides, polio, multiple sclerosis, etc.

Drugs and Non-Bacterial Toxins These present morphine, nicotine (in large quantity), bromides, the barbiturates and other sedative agents. Many industrial poisons may cause loss of potency: vaporous, inhalatory or skin-absorptive.

General Discussion on the Problem It should not be forgotten that the male climacteric, in the physiologic and gonodal sense of the term, does not occur usually until well on into senility.

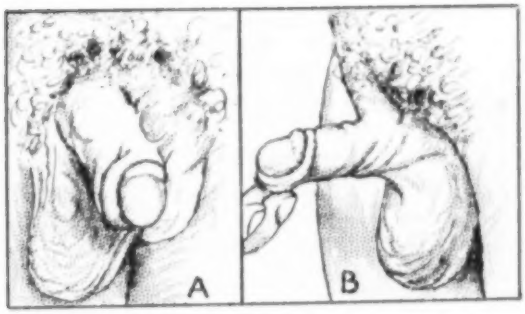


Fig. 2. Immobile penis caused by dense scar tissue and fibrous bands keeping penis in close proximity to the left thigh, relieved by a cartilage graft inserted to replace the fibrotic left corpus cavernosum.

A. Anterior view showing marked deviation of penis to the left.

B. Showing appearance of penis following insertion of cartilage graft.

It is extremely rare in the third decade;[5] but may be seen occasionally in the fourth and the fifth decade as a progressive loss of function as the drop in germinal and hormonal activity begins.

Actually, the male climacteric may now be differentiated from psychogenic impotence (where it is necessary to do so in the obscure case) by the use of urine gonadotropic assays, where it is decidedly elevated in the climacteric but normal in the latter. Further work[3] reveals that the normal average secretion of androgenic substances are zero plus to the age of eight years in the male, then rise from 6 to 5 capon units (C.U.) in 24 hours to the age of 20. After this age, it stabilizes itself around 10-12 C.U. through the 35th year. It then begins to fall by 1/5th C.U. per annum through the sixties, approximately.

On the other hand, gonadotrophin rises to 6 R.U. excreted in 24 hours in the ages from 8 to 15. It remains at this level until the sixties when it begins to rise into the climacteric average of about 15 R.U. in 24 hours.

Therefore, it can be seen why writers, such as Mason[2] can state almost dogmatically today that derangement in sexual function runs a parallel percentage to psychoneurosis in the population. He further cites a 10% sexual loss in patients suffering from a headache-vertigo syndrome. Also, many other problems, including angina pectoris,[2] appear to be tied up together with impotentia and ignorance of aberrations in coitus and the necessary excitations of the love-play.

Many of the problems of potency appear to be related to the sufferer of premature ejaculation, often along with tachycardia, hypertension, syncope, enuresis, and somnabulism.

In a recent, pithy, well-written paper[1] Tuthill describes the problems of three psychologic aberrations of impotentia that may be first treated physiologically. They were listed as: 1. insufficient erection, 2. premature ejaculation and 3. as failure of ejaculation.

Insufficient erection appears to him to be related to the taboos—personal or social—of thoughts or feelings which can only be allayed partially by impotence. Premature ejaculation must take place in the sufferer who must "let fly, let go," otherwise he will gradually fail and fall into the abyss of the anxiety of failure.

In this group, the use of a vaso-dilator of the urethra may prove helpful as may amphetamine sulfate, strychnine, arsenic, yohimbine in various combinations. The employment of excitatory fantasy, he states, may help.

The primary cause of failure in this group is a faulty development of sexual reflexes due fundamentally to over-concern with the restraints of society. Better sex education by physicians is necessary. He feels that mild masochism, Sadism, fetishism or transvestism, when adequately understood and not harmful to others, should be allowed by society . . . since they are related to symbolistic needs of repressive training. Feeling inadequate and anxious, our culture adds guilt to their burdens. They fail then in their potency as heterosexual individuals!

Strauss[45] relates the strength or feebleness of the sexual desire in some cases to congenital determination, both in its start and in its decline. He states emphatically that the popular equation of general virility with potency is a fallacy that has persisted for many generations—as is the size of the genitalia to potency. He believes that many adolescents have agonizingly talked themselves into phobic impotence because of these erroneous beliefs.

Categories of Impotence (1) Honeymoon impotence, because of the breakdown strain of masculine justification, (2) Masturbation anxieties, recrudescent and allied to failure except when alone, (3) Perineal components associations of the sex impulse (sadomasochistic vacillation, homosexual memories, etc.), (4) Unresolved incestuous attachments, e.g. identification with mother or sister (therefore, he cannot—this is not mere Freudian whimsies, having been proven over and over again with many cases), (5) Impotence with the "Respected, loved woman" only—yet not with others, (6) Impotence related to feelings of being unworthy—usually related to (4) and (5), (7) soldier's impotence, seen especially during the war years with hit and miss furloughs ("You're home—now prove yourself."), (8) Depression-syndrome impotence: a vicious cycle, with the failure driving the male into further depression, (9) Impotence, due to inability to ejaculate: related to fear of wife's pregnancy, narcissistic inability "to give" and usually associated with constipation, (10) Fatigue Impotence—seen in men married to their professions—and observed in doctors!

Methods Of Investigation All factors mentioned in this article need to be considered carefully in the proper evaluation. A proper, non-prudish balance must be given as objectively as possible to the scrutiny of familial, anatomical, physiologic, and pathological disturbances of the organic systems and the psychological makeup, peculiar and unique to this one unfortunate individual. The routine must be systematized and comprehensive: and this alone, conducted sympathetically and without moral judgments, may be partially therapeutic.

A complete medical history is important. Frank answers to the questions relating to desire, power and sustenance of erection, prematurity or prolongation of the ejaculation and its duration and propulsion, possibilities of pain or pressure, etc. need to be obtained. The current and past marital status of the patient should be elicited, as well as any abnormal sexual practices.

It is important to ascertain the social background, occupation, economic factors, the use and quantity of drugs, alcohol, contact or inhaled chemicals, hereditary familial disorders and degenerations (so ably emphasized by W. C. Alvarez[1]), and the general emotional makeup of the patient. Any one of these may prove to be the clue-wedge opening up the problem to therapy.

The general physical attributes need itemized study. The amount, proportion and placement of fat should be noted: as is also true of the individual's hair. The penis, the scrotum, the perineum, the prostate, and the secretions should be checked. Laboratory data, and sometimes x-ray and cystoscopic illumination may prove helpful in determining possible hindrances to the complex, relays and switches of the *Ultima Thule*[20, 31, 32, 14, 21, 22].

Treatment Stafford-Clark makes the interesting, statistical observation[44] in his study, that 45% of husbands who were queried stated that they were not satisfied with their sexual capacities. The actual incidence of dissatisfaction is not really known. His dogmatic generalization is that 90% of this problem is psychogenic in nature.

The largest number can and should be helped by the general practitioners whom they trust. This is so because most are caused by unnecessary burdens of guilt, anxiety or apprehension inhibitions based on family and social taboos. These are not deep personality schisms or scarring of a crippling nature.

The family doctor's time is needed for this. The patient must be made to understand and be willing to pay for this previous time.

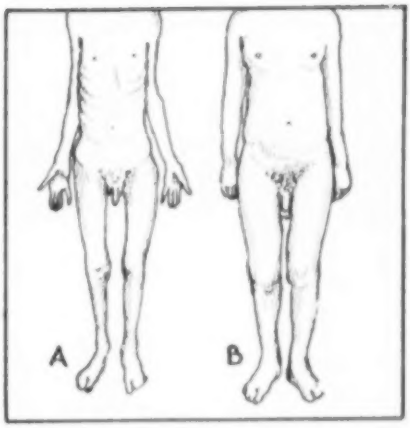


Fig. 3. Schematic drawing of patient before and after prefrontal lencotomy.
A. Before operation well-marked hypogonadism and emaciation.
B. Four months after operation showing marked improvement in genital size and obesity.

Of course, if physical or hereditary or marked endocrine disorders are found, it will be advisable to go further afield. In some cases, a specialist's aid should be enlisted—but not to take over.

Fifty per cent of impotentia under the age of 35 years should often begin their cure after the first or second such visit to the listening, objective yet sympathetic, family doctor. The release of guilt or anxiety is almost palpable.

Beyond this point, some further training of the G.P. is needed, but not difficult to acquire in graduate sessions at county or state medical society or university levels. The giving of advice is less healing than assurance that the patient is exhibiting behavior patterns not much different than his brothers in the same culture, and in the same social stratum.

The patient must be given a chance to talk his problem out. Interruptions should be few.[44] A separate discussion should be attempted with the sexual partner. The patient needs to be accepted as he is—and then adequately related to the times and the places of his environment. With this help, a further resistant 25-30% of cases can be happily cured in 6-12 interviews.

However, it is best to promise these patients little in advance except encouragement to continue. Most of them have tried every other approach and have failed with the neurasthenia of anxiety.

Operative interference for congenital defects has been employed by Lowsley and others[24, 25, 26, 43] utilizing plastic interference to blood return of the corpora, cartilage grafts for reinforcing erectile tissue, plastics of various kinds, etc.

Success has been claimed by these workers in selected cases of erectile failure associated with trauma, disease, or chemical or masturbatory injuries.

Aphrodisiacs of various types have been marketed with varying success. Dietary changes, especially the ingestion of animal proteins, have also been credited as being helpful in some nutritional disturbances type of impotentia.

Physiotherapy of various modalities have been employed by some, along with prostatic massage. Vitamin E in large doses has also been used, based on animal experiments on fertility.

Some workers have prescribed anesthetic ointments to be massaged into the penis for premature ejaculations—or oral sedation of the barbiturate group.

In hypogonadism, the treatment is relatively simple and straightforward—if not always successful. It is the use of various testosterone extracts, along with some thyroid desiccated tablets in the lethargic individual. Many of these individuals show a reduced metabolic rate.

It must not be forgotten that many of these individuals often reveal a constellation of related general organic disturbances, such as secondary anemia, circulatory disorders, intestinal amotility with obstipation, etc. It will be important to relieve these associated conditions by the various, recognized hematinics, antispasmodics, musculotonic laxatives, e.g. cascara, etc., vitamins, dietary supplements, occasional change of pace, place, play and work.

In closing, it may be important to restate the following, urgent and cogent quotation:[45] "No medical man can afford to be ignorant of the etiology and nature of this sexual disability and he should always be prepared to give a sympathetic hearing and informative advice to these unfortunate patients . . ."

Bibliography

1. Alvarez, W. C. Impotence. Clinical Medicine, v. 54, May, 1937, pp. 158-159.

2. Benjamin, H. Endocrine aspect of problem: 39 cases. Urologic & Cutaneous Review, v. 50, March, 1946, pp. 139-143.

3. Belfrage, S. H. Medical aspects of law on nullity of marriage [on grounds of sexual incapacity.] Medical Press, v. 211, June 7, 1944, pp. 358-361.

4. Bergler, E. Newer genetic investigations. Bulletin, Menninger Clinic, v. 11, March, 1947, pp. 50-59.

5. Bergler, E. Short genetic survey of psychiatric impotence. Psychiatric quarterly, v. 19,

July, 1945, pp. 412-437.

6. Bergler, E. Short genetic survey of psychic impotence. Psychiatric Quarterly, v. 19, October, 1945, pp. 657-676.

7. Bergler, E. Some a-typical forms of impotence and frigidity. Psychoanalytic Review, v. 41, no. 1, January, 1954, pp. 29-47.

8. Biskind, M. S. Relation of nutritional deficiency to impaired libido and potency in male. Journal of Gerontology, v. 2, October, 1947, pp. 303-314.

9. Cantor, A. J. Hemorrhoidal-prostatic impotence syndrome. New York State Journal of Medicine, v. 46, July 1, 1946, pp. 1455-1456.

10. Chappell, B. S. Relief of impotency by cartilage implants; presentation of technique. Journal, South Carolina Medical Association, v. 48, February, 1952, pp. 31-34.

11. Collings, C. W. Therapy. Transactions, Western Section, American Urological Association, v. 13, 1946, pp. 97-100.

12. Ellasberg, W. Disorders of male sexuality as encountered in practitioner's office. Psychiatric Quarterly, v. 18, October, 1944, pp. 567-581.

13. Elkasberg, W. Marital disorders erroneously called male sexual disorders. Medical Women's Journal, v. 51, September, 1944, pp. 27-29.

14. Fletcher, P., & Walker, K. Non-sexual factors in impotence. Medical World, v. 78, no. 6, June, 1953, pp. 596-601.

15. Heller, C. G., & Myers, G. B. Male climacteric; its symptomatology, diagnosis and treatment; use of therapeutic test with testosterone propionate (androgen) and testicular biopsies in delineating male climacteric from psychoneurosis and psychogenic impotence. Journal American Medical Association, v. 126, October 21, 1944, pp. 472-477.

16. Hemphill, R. E. Return of virility after prefrontal leukotomy (in case of obsessional neurosis) with enlargement of gonads. Lancet, v. 2, September 9, 1944, pp. 345-346.

17. Hirsch, E. W. Sexual impotence: plea for more descriptive terminology. Medical Record, v. 157, October, 1944, pp. 611-612.

18. Hulse, W. C. Management of sexual conflicts in general practice. Journal American Medical Association, v. 150, November 1, 1952, pp. 846-849.

19. Jenner, S. W. Unusual side reaction in antihistaminic therapy. Annals of Allergy, v. 8, May/June, 1950, pp. 407.

20. Keshin, J. G., & Pinck, B. D. Impotence. New York State Journal of Medicine, v. 49, February 1, 1949, pp. 269-272.

21. Loewenstein, J. Disorders of erection, no. 1. Marriage Hygiene, v. 1, August, 1947, pp. 15-40.

22. Loewenstein, J. Disorders of erection, no. 2. Marriage Hygiene, v. 1, November, 1947, pp. 92-97.

23. Loewenstein, J. T. Mechanotherapy; recent experiences with C. T. (coitus-training) apparatus. Medical Press, v. 211, June 14, 1944, pp. 381-384.

24. Lowsley, O. S., & Rueda, A. Further experience with an operation for the cure of certain types of impotence. Journal International College of Surgeons, v. 19, no. 1, January, 1953, pp. 69-77.

25. Lowsley, O. S., & Cangelosi, J. T. Ten years' experience with operation for cure of certain types. Southern Medical Journal, v. 39, January, 1946, pp. 67-69.

26. Ma, J. Y. C. Lowsley plastic operation for cure of certain types of sexual impotence with 2 case reports. Chinese Medical Journal, v. 67, March, 1949, pp. 143-146.

27. Mason, I. Headaches and vertigo and their correlations to derangement of sexual function. Ohio State Medical Journal, v. 41, February, 1945, pp. 132-136.

28. Mellcow, M. M. Coitus impotence and angina pectoris. New York State Medical Journal, v. 45, June 15, 1945, pp. 1325-1328.

29. Michael, S. T. Impotence during electric shock therapy. Psychiatric Quarterly, v. 25, January 1, 1951, pp. 24-31.

30. Miller, S., & Mason, H. L. Excretion of 17-ketosteroids by diabetics. Journal, Clinical Endocrinology, v. 5, May/June, 1945, pp. 220-225.

31. Munro, D.; Horne, H. W., Jr., & Paull, D. P. Effect of injury to spinal cord and cauda equina on sexual potency of men. New England Journal of Medicine, v. 239, December 9, 1948, pp. 903-911.

32. Nayar, R. Impotence in the male. Indian Medical Journal, v. 43, October, 1949, pp. 274-280.

33. Pedersen-Bjergaard, K., & Tonnesen, M. Sex hormoneanalysis; excretion of sexual hormones by normal males, impotent males, polyarthritics and prostatics. Acta Medica Scandinavica, supplement no. 213, v. 131, 1948, pp. 284-297.

34. Powers, D. F. Psychic impotence in the male. West Virginia Medical Journal, v. 50, no. 1, January, 1954, pp. 48-50.

35. Rabiner, A. M., & Rubinstein, H. S. Dorsal nerve of penis as factor in potency. Transactions, American Neurological Association, v. 70, 1944, p. 177.

36. Reed, W. A., & Lally, J. F., Jr. A clinical trial with testosterone cyclopentylpropionate. Journal, Louisiana Medical Society, v. 105, no. 5, May, 1951, pp. 172-174.

37. Rosecan, M.; Glaser, R. J., & Goldman, M. L. Orthostatic hypotension, anhidrosis and impotence. Circulation, v. 6, July, 1952, pp. 30-40.

38. Rose, R. B., & Kimbrough, J. C. Study of incontinence and impotence following prostatic surgery. Military Surgeon, v. 108, June, 1951, pp. 481-483.

39. Schapiro, B. Potency disorders in the male; a review of 1960 cases of premature ejaculation. Harefuah, v. 45, no. 2, July, 1953, pp. 39-41.

40. Schwartz, H. B. Prostatic-hemorrhoidal impotence syndrome. Journal Medical Society, New Jersey, v. 44, September, 1947, pp. 371-373.

41. Schwartz, N. H., & Robinson, B. D. Due to methantheline bromide (quarternary ammonium compound.) New York State Journal of Medicine, v. 52, June 15, 1952, pp. 1530.

42. Segaloff, A. Testicular dysfunction: diagnosis and treatment. American Practitioner, v. 1, September, 1946, pp. 15-22.

43. Solomon, A. A., & Karleen, C. I. Case following trauma to corpora cavernosa relieved by cartilage grafts. Journal of Urology, v. 58, October, 1947, pp. 289-294.

44. Stafford-Clark, David. The etiology and treatment of impotence. Practitioner, v. 172, no. 1030, pp. 397-404, April, 1954.

45. Strauss, E. B. Impotence from psychiatric standpoint. British Journal of Medicine, v. 1, March 25, 1950, pp. 697-699.

46. Therapy: secrets from India—via Denver: Victor Croley plays old game and loses: Bureau of Investigations. Journal American Medical Association, v. 128, May 5, 1945, p. 51.

47. Walker, K. Causation. Practitioner, v. 158, April, 1947, pp. 289-294.

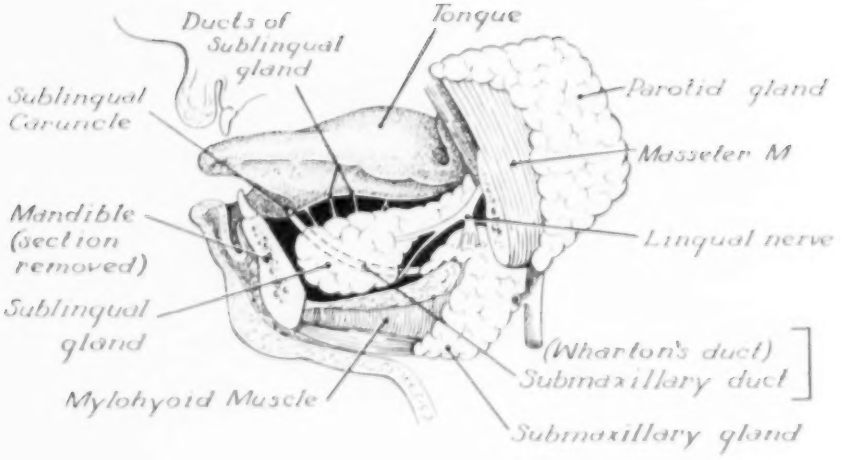
48. Watkins, J. G. Hypnoanalytic treatment of case. Journal of Clinical psychopathology, v. 8, January, 1947, pp. 453-480.

49. Wilder, J. Genital and sphincter symptoms in multiple sclerosis: frequency, course and response to pancorphen. Diseases of the Nervous System, v. 15, no. 7, July, 1954, pp. 200-206.

50. Wolbarst, A. L. Gynecic factor in causation of male impotence. New York State Journal of Medicine, v. 47, June 1, 1947, pp. 1252-1255.

51. Tuthill, J. F. Impotence. Lancet, Jan. 15, 1955, pp. 124-128.

Clini-Clipping



Schematic drawing of major salivary glands showing their location (part of parotid gland and Stenson's duct not shown).

Polygen Z-49

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Polygen Z-49 is a new composition of many antigens to be used for the purpose of sensitizing susceptible particles causing asthmatic attacks and allergic reactions. It is currently limited to further investigational use in the treatment of asthma and other allergies. Preliminary studies made with it during the last decade seem to indicate some very promising results.

Method of Preparation Polygen Z-49 originally was prepared directly from the sputum of asthmatic patients, preferably collected during an attack. The sputum was digested by a fermentation process, extracted, and filtered. The extract was combined with a nonspecific antigen derived from beef heart and the mixture was standardized by a complement fixation technique. This technique is based upon the fact that Polygen will quantitatively inactivate or "fix" serum complement.[1]

Later experiments indicate that a universal preparation is made by substituting the sputum collected from patients suffering from asthma, by a Trichosporon filtrate (Zuccala's method), lactic acid, deproteinized blood, and in the media used to culture the Trichosporon, raw honey is used. Although the autogenous product may be preferable in stubborn cases, the new composition is practical and satisfactory.

Theory of Action It is possible that Polygen Z-49 inactivates in *vivo* some offending substances involved in the chain of biochemical reaction leading to the asthma attack. It is also possible that Polygen initiates or stimulates the generation by the body of some substance which, in turn, acts to block the biochemical reactions leading to the asthma attack. However, while this product is showing remarkable promise, according to clinical data collected this far, the exact mechanisms of Polygen in the biochemistry of asthma have yet to be established. In other words, the value of this preparation is being established empirically rather than by *a priori* reasoning from theory.

In some correspondence from previous investigators of this Polygen, I learned that Nicholas Milella, M.D., F.A.C.A., in one of his lectures, presented this theory about Polygen:[2] "Foreign substances enter the body, or may be produced in the body by chemical or bacteriological reaction such as atopen, allergens, reagin, H-substances or whatever name is applied. Some allergists prefer to say that foreign mat-

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ter produces histamine-like substances with the result of stimulating the parasympathetic (vagus) nerves and causing a variety of discomforts to the patient." The present therapeutic measures are based on the theory of desensitizing the human body or producing immunity from the cause of the ailment. Present day remedies consist predominantly of a protein-base substance, which does not entirely desensitize the body. It may cause little relief or temporary relief but, fundamentally, it loads the body with more foreign proteins, whose after effects have not been ascertained.

Instead of using the old method which assumes to desensitize the body, it may be possible to sensitize the minute particles which cause the asthmatic attacks. This would allow the natural complement to split or break down this substance and the body would be free from foreign substances. The following is a specific example: When working with the Wassermann test, if sheep cells are not sensitized by means of an anti-sheep amboceptor when adding the complement, there would not be any hemolysis. This is easily demonstrated in *vitro*. However, if the sheep cells are sensitized by adding either human, or guinea pig complement, a complete hemolysis will occur. This indicates that the cells are susceptible to complement and easily broken. This also proves that a complete or partial hemolysis depends upon the amount of sensitizing or lysin introduced into the sheep cell solution. Since this reaction can be demonstrated in *vitro*, why can't we assume the same effect in *vivo*? Considering the possibility of this theory, allergists from many countries are now engaged in further research with this new concept of Polygen Z-49. It was Dr. Albert Carradory who published the formula of Polygen and who interested many immunologists, who were curious to know what part of the composition acted in blocking antibodies and preventing the human body from developing immunity after a few injections, similar to many other vaccines presently in use.[3]

Advantages Over Older Treatments

A. Minimizing of side effects. (Clinical studies to date indicate a minimum of discomfort due to side effects.)

B. Effective relief in many cases. (A fairly high percentage of patients treated thus far with Polygen Z-49 have experienced either complete remission or marked improvement.) Polygen is not a quick relief and takes several months before results are noticeable. Neither has it been classified as a wonder drug. It is a new composition which many scientists wish to investigate further.

Dosage and Method of Administration Polygen is administered by subcutaneous or intramuscular injections, preferably intramuscular injection only. The following plan is suggested for most cases but may be varied at the discretion of the attending physician.[4] Begin with a dose of 0.4 cc. and increase this by 0.2 cc. every other day until a 1 cc. dose is reached. If at any time the injection is followed by an erythema, an appreciable swelling or any other marked reaction, maintain the same dose at the time of the next injection or slightly decrease it. As soon as the new dose causes no untoward response, again increase the dose by 0.2 cc. for the following treatment. Do not increase the dose beyond 1 cc. but maintain this dose once it has

been reached. Continue to administer every other day until a definite improvement is observed. Then gradually increase the interval between injections to once a week and eventually to a maintenance dose of once a month.

History In 1941, George S. Zuccala, Sc.D. of Huntington Medical Laboratories, W. F. Hollander, Ph.D., of Carnegie Institute, and Carl V. Granger, M.D., of Huntington Station, Long Island, conceived the idea of developing an antigen capable of treating asthmatic patients. Zuccala, the serologist in the group, began to investigate a complement fixation reaction in an attempt to develop a desensitizing treatment for bronchial asthma. After several years of research he discovered that a preparation obtained from the sputum of an asthmatic patient quantitatively inactivates or "fixes" serum complement. He further observed that the sputum collected during an attack provided a preparation with a high fixation titer and that the titer, moreover, varied from patient to patient. After further research, Zuccala developed a method for standardizing his preparation by means of a complement fixation technique which gives a tolerance and potency reaction. Dr. Hollander then tested the preparation on laboratory animals for any evidence of anaphylaxis or other untoward side effects. After all the animal tests were performed, the formula and process was recorded with the Federal Food and Drug Administration for evidence that a certain preliminary test was being made according to the rules and regulations of the law. Dr. Carl V. Granger then tested the Polygen on human patients for its effectiveness in relieving bronchial asthma. The first patients yielded some striking results. This encouraged other physicians to give it a trial. By February 1947 the first professional paper on this new product appeared in print in the United States.[3] This paper reported very briefly a series of 100 cases (practically all chronic) treated with the new preparation. The results were given as follows: 65% symptom free, 25% marked improvement and 10% showing varying degrees of lesser improvement.

Meanwhile, interest in the new treatment had spread to other countries. Dr. N. Agadjanianets and his associates in Paris, France tried the method and after a year of research published a paper on the subject in which he expressed high enthusiasm.[4] In Italy Prof. P. St. George,[5] a well known allergist and professor at the Milan University Medical College together with his colleagues, conducted numerous clinical trials. In November 1949, Prof. St. George, collaborating with Prof. Cesare Frugoni, Dean of the Medical University of Rome, Italy published a textbook on allergy.[6] In this book the authors described the product and also assigned it the name Polygen Z-49.

In January, 1950, Prof. St. George published a paper,[7] in which he discussed in considerable length Polygen Z-49 and its role in treating asthma and relieving other allergies. He also described 21 cases in which "other methods of treatment, including sedation, was forsaken," prior to treatment with Polygen. Of these 21 cases, after treatment, 11 experienced disappearance of the symptoms, 7 received marked relief and 3 received little or no relief. Many of these were chronic cases. One particular case of long duration (30 years), Prof. St. George stated, was a challenge. Prof. St. George concluded: "It is re-

markable that at least 85% of the cases treated in the Salice-Terme Clinic showed remarkable relief, and should we even cut down the percentage of disappearance of symptoms, it is still a fact that Polygen is distinctly more effective and safer than any available desensitizing substance."

In the United States equally enthusiastic reports are accumulating. As this report goes to press, clinical data on Polygen is being collected by qualified allergists at hospitals in many parts of the United States. Among them are: St. John's Episcopal Hospital, Brooklyn, L. I., N. Y., by Dr. Chapel Emerson Carter; St. John's Riverside Hospital, by Dr. John P. Foland; Mt. Sinai Hospital, Chicago, Ill., by Dr. A. L. Terman; Mt. Sinai and Hartford Dispensary, by Dr. George Hurwitz, and St. Francis Hospital in Hartford, Conn., by Dr. V. P. Cenci (author).

A large number of physicians are now using Polygen in private practice. Polygen is limited by Federal Law (Section 505 of the Food and Drug and Cosmetic Act). It is dispensed only upon the prescription or signed statement of a licensed medical doctor.

How to Obtain Polygen Z-49

Polygen is prepared by the Farmington Biological Laboratory under the manufacturing license #103. Any pharmacy may procure it for physicians direct from the laboratory in the state of Connecticut only. Outside of Connecticut, physicians can obtain the medicine by signing the application of "Statement of Investigator" to show that the medicine is to be used for experimental purposes only.

Acknowledgments Chief Consultant—Lawrence W. Smith, M.D., a graduate of Harvard Medical School, was consultant on epidemic diseases to the Secretary of War during World War II. He is a member of a number of national research societies. He is senior author of the textbook, *Essentials of Pathology* (Smith and Gault) and a contributor to numerous scientific papers, chiefly in the field of infection and cancer. He is now in private consultant practice.

References

1. Zuccala, G. S., M. T., Journal of the American Medical Technologist, 8, (1947).

2. Milella, N., M.D., lecture given at Italian Allergists Association, at Bari, Italy on January 30, 1953.

3. Corradory, B. R., M.D., International Correspondence Society of Allergists, series 15, 81 (1952).

4. St. George, P., M.D., Avvenire Sanitario (Future Medicine) 1 (1950).

5. Ciafone, F. C., M.D., Medical Record, 360, 78 (1947).

6. Agadianianets, N., M.D., Journal de Medicine de Paris, 4, 66, (1949).

7. Chief Investigator of Polygen Z-49: Piero St. George, M.D., F.A.C.A., F.I.A.A., associate Professor of Medical Pathology, University of Milano School of Medicine, Professor Pavia, University Medical College, Secretary of the Italian Allergy Association, "member of the editorial board of **Quarterly Review of Allergy and Applied Immunology;**" recipient of the Prize of the Royal Academy of Italy (1937) for the work **L'Asma, Bronchiale Climallergico;** author of the book **Principi Di Allergia Clinica,** Red Publishing Co., Milano; he is founder and director of the Allergy Clinic at Salice Terme, Italy.

8. Sangiorgi (St. George) Piero and Prof. Cesare Fruguni, Principi di Allergia.

9. St. George, P., M.D., and associates of the Italian Allergists Society, I Quaderni dell' Allergia. Report of First International Con-

gress of Allergists, Zurich, Switzerland, 9, 209 (1951).

Carter, Chapel E., M.D., Quarterly Review of Allergy and Applied Immunology, 4, 204 (1950).

Sticotti, S., M.D. and Antonio Manino, M.D., Allergia-Tome 2, 43, (1951).

Ibid., Modern Medicine, "Antigen for Asthma" 26, (1951).

Other investigators include the following doctors: J. P. Foland, C. E. Carter, J. Harris, C. V. Granger, G. Hurwitz, L. A. Tarman, H. J. Wilson and L. W. Smith, all United States.

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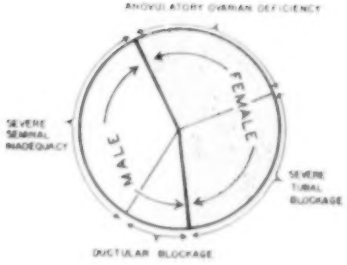

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2. Reduced speed, S shape "undulatory tactile phase."

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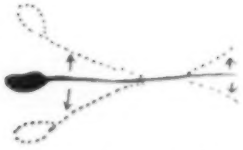
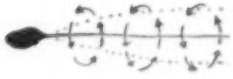


4. Rapid but spiral and screw-like, "rotary swimming phase."



5. Loss of balance of middle and upper tail, "pendulum" swimming phase.

Swimming phases of spermatozoa. Phases 1-3 are normal in fresh specimens. Phases 4-5 are abnormal in fresh specimens and indicate impaired ability to fertilize.

A New Non-Narcotic Antitussive Agent

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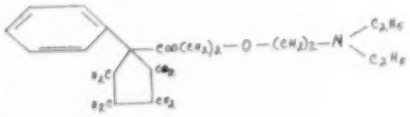
Almost every practitioner is faced daily with the problem of prescribing an antitussive medication for one or more of his patients. Ideally, such a drug should have certain properties: selective depression of the cough reflex, absence of such undesirable side effects as drowsiness, constipation or irritation of mucous membranes as well as freedom from any narcotic or toxic potentialities. Besides these desirable attributes, an antitussive compound must have sufficient palatability to be well accepted and, thus, taken by the patient as directed. It is the purpose of this paper to report on 44 cases, suffering from both productive and nonproductive coughs of varied etiology, who were treated with a new non-narcotic antitussive agent, Toclase.* From the results of this preliminary study, it would appear that Toclase possesses the above-mentioned qualities yet lacks the unwanted characteristics of many of the currently used cough remedies, particularly codeine.

*Toclase (brand of carbetapentane citrate) Pfizer Laboratories, Chas. Pfizer & Co., Inc., Brooklyn, New York.

Pharmacology of Toclase Toclase (carbetapentane citrate) is a recently discovered drug which has the chemical designation 2-(2-diethylaminoethoxy)-ethyl-1-phenylcyclopentyl-1-carboxylate and the structural formula as shown below.



The prime feature of this agent is its selective action on the cough reflex. This depression of the tussive mechanism is probably mediated through the action of Toclase on the cough reflex center located in the medulla. There is also laboratory evidence to indicate that Toclase is imbued with some local anesthetic activity as well as antispasmodic properties exceeding those of atropine. Pharmacologic studies have revealed no untoward effects of this medication with respect to acute or chronic toxicity, the drug having a wide margin of safety.[1] Further, extensive

clinical trials, both here and abroad, have confirmed the fact that Toclase is neither habit forming nor capable of producing addiction.[2,3]

There are three different dosage forms of Toclase: (1) tablets of 25 mg.; (2) syrup containing 7.25 mg. of Toclase in each teaspoonful; and (3) expectorant compound containing 7.25 mg. of Toclase and 16.67 mg. of terpin hydrate in each teaspoonful of an aromatic demulcent vehicle. While the syrup dosage form contains dextrose, the expectorant compound is sugar free and, therefore, suitable for use in diabetic patients.

Dosage The recommended dosage schedules of Toclase are as follows:

Adults and children over 12

15-30 mg. three or four times a day (2 to 4 teaspoonfuls of syrup or expectorant compound or 1 tablet)

Children, ages 4-12

7.25 mg. (1 teaspoon) t.i.d. or q.i.d.

Children under 4

3.12 mg. (½ teaspoon) t.i.d. or q.i.d.

Clinical Material In this study 44 patients were treated for both nonproductive and productive coughs of varying etiology (infectious, allergic, irritant) with one of the different dosage forms of Toclase. Included in this group were males and females ranging in age from 11 months to 60 years and of differing racial backgrounds.

As will be noted in Tables 1, 2 and 3, the results of therapy with respect to inhibition of the cough reflex were uniformly excellent, despite the inciting cause of the paroxysms and irrespective

TABLE 1
RESULTS OF THERAPY WITH TOCLASE TABLETS

Diagnosis	Age	Productive	Non-Productive	Dosage	Duration (Hours)	Inhibition of Cough Reflex	Comparison with Previous Anti-Tussive Medications*	Side Effects
1. Erythema multiforme	60	X		15 mg. q.i.d.	3-4	excellent	+	0
1. Acute coryza	1½		X	4 mg. q.i.d.	2-3	excellent	+	0
3. Allergic nasopharyngitis	27	X		15 mg. q.i.d.	4	excellent	+	0
4. Acute coryza	10	X		15 mg. q.3 h.	3	excellent	+	0
5. Acute coryza	4	X		7.5 mg. q.4 h.	2	excellent	+	0
6. Acute coryza	38	X		15 mg. q.3 h.	3	excellent	+	0
7. Acute coryza	45	X		15 mg. q.3 h.	3	excellent	+	0
8. Acute coryza	15	X		15 mg. q.3 h.	3	excellent	+	0
9. Asthmatic bronchitis	60		X	15 mg. q.3 h.	3	excellent	+	0
10. Allergic nasopharyngitis	34		X	22 mg. q.i.d. & h.s.	3-4	excellent	+	0
11. Acute coryza	13		X	15 mg. q.4 h.	3	excellent	+	0
12. Acute coryza	15		X	15 mg. q.4 h.	3	excellent	+	0
13. Acute coryza	35		X	15 mg. q.i.d.	3-4	excellent	+	0
14. Acute coryza	11	X		15 mg. q.4 h.	3-4	excellent	+	0
15. Acute coryza	13	X		15 mg. q.i.d.	3-4	excellent	+	0
16. Irritative cough (tobacco)	62	X		15 mg. q.i.d.	4	excellent	0	0
17. Asthmatic bronchitis	52		X	15 mg. q.i.d.	3-4	excellent	+	slight nausea
18. Asthmatic bronchitis	38		X	15 mg. q.i.d.	2-3	excellent	+	0

*Superior to (+) Equal to (0) Inferior to (—)

of the dosage form used. Alleviation of the cough was achieved within minutes after taking Toclase and this salutary effect was maintained in the majority of patients around 4 hours. Tussive problems with an allergic basis noted not only a marked decrease in the frequency and severity of the coughing episodes but also frequently observed amelioration of the primary hypersensitivity signs and symptoms as wheezing, nasal congestion and sneezing. This would seem to indicate that, clinically, Toclase possesses definite anti-

TABLE II
RESULTS OF THERAPY WITH TOCLASE SYRUP

Diagnosis	Age	Productive	Non-Productive	Dosage	Duration (Hours)	Inhibition of Cough Reflex	Comparison with Previous Anti-Tussive Medications*	Side Effects
1. Allergic nasopharyngitis urticaria	35		X	22 mg. q.3 h.	3-4	excellent	+	Slight drowsiness. Cleared 2nd day while still on medication.
2. Acute coryza	1		X	4 mg. q.4 h.	4	excellent	+	Slight drowsiness 1st day. Cleared 2nd day while on medication.
3. Acute coryza	21	X		20 mg. q.4	3-4	excellent	+	—
4. Acute coryza; bronchial asthma	50		X	20 mg. q.i.d. & h.s.	5-8	excellent	+	0
5. Asthmatic bronchitis	14		X X	15 mg. q.i.d. & h.s.	4	excellent	+	Slight drowsiness 1st day. Cleared 2nd day while on medication.
6. Irritative cough (tobacco)	44		X	15 mg. q.3 h.	1	fair	none used	0
7. Acute coryza; hay fever	30		X	15 mg. q.3 h.	3-4	excellent	+	Slight drowsiness.
8. Asthmatic bronchitis	16		X	15 mg. q.i.d.	4	excellent	+	Rash on thigh. Cleared while on medication.
9. Asthmatic bronchitis	35	X		30 mg. q.i.d. & h.s.	4	excellent	+	0
10. Acute coryza & bronchitis	34	X		30 mg. q.i.d. & h.s.	4	excellent	+	0
11. Acute coryza	8		X	7 mg. q.i.d. & h.s.	3	excellent	+	0
12. Acute coryza	12	X		14 mg. q.i.d. & h.s.	3	excellent	+	0
13. Acute coryza & irritative cough (tobacco)	24		+	20 mg. q.i.d. & h.s.	4	excellent	+	0
14. Acute coryza	53	X		30 mg. q.i.d. & h.s.	4	excellent	X	0
15. Acute coryza	31		X	30 mg. q.i.d. & h.s.	3	excellent	+	papulocry-thematous pruritic rash over body on 4th day.
16. Acute coryza	28			15 mg. q.i.d.	4	excellent	+	0

* Superior to (+) Equal to (0) Inferior to (—)

spasmodic activity. Where pharyngeal soreness and discomfort were present, the local anesthetic action of Toclase contributed almost immediate relief for upwards of 3 hours. In all but 1 case, Toclase was considered superior in every respect to any previously taken anti-cough remedy which included many of the commonly used over-the-counter and ethical preparations.

A striking feature of this study was the fact that all of the patients, without exception, liked the flavor of the liquid forms of Toclase, remarking in many instances that it was extremely pleasant to take. This is rather remarkable since several of these persons were quite neurotic and had previously complained bitterly about other antitussive medicaments prescribed for them.

Side Effects The side effects occurring in this case series following the administration of Toclase were minimal. In 4 patients, slight drowsiness was noted on the first day but was not incapacitating. Except in 1 instance, this mild sedation disappeared even though the Toclase was not withdrawn. This would make it appear that the drowsiness was not a true side effect but was, in all probability, a manifestation of the disease process itself. One highly emotional woman complained of episodes of slight nausea for the first 24 hours. There were 2 patients who developed skin rashes, one of which had complete clearing of the rash despite continuation of therapy. The second case probably represents a true drug rash since it erupted on the fourth day of treatment and cleared only on discontinuing the drug.

TABLE III
RESULTS OF THERAPY WITH TOCLASE EXPECTORANT

Diagnosis	Age	Productive	Non-Productive	Dosage	Duration (Hours)	Inhibition of Cough Reflex	Comparison with Previous Anti-Tussive Medications*	Side Effects
1. Asthmatic bronchitis	44		X	25 mg. q.i.d.	3-4	excellent	+	—
2. Acute coryza	31		X	25 mg. q.i.d.	4	excellent	+	0
3. Asthmatic bronchitis	25	X		25 mg. q.i.d.	3-4	excellent	+	0
4. Asthmatic bronchitis	33		X	25 mg. q.i.d.	4-5	excellent	0	0
5. Acute coryza	46		X	25 mg. q.i.d.	4-5	excellent		Slight drowsiness
6. Allergic nasopharyngitis	49		X	25 mg. q.i.d.	4	excellent	+	—
7. Allergic nasopharyngitis	50		X	25 mg. q.i.d.	4	excellent	+	0
8. Allergic nasopharyngitis bronchial asthma	19		X	25 mg. q.i.d.	3-4	excellent	+	0
9. Allergic nasopharyngitis	12		X	25 mg. q.i.d.	3-4	excellent	+	0
10. Asthmatic bronchitis with secondary bacterial infection treated with penicillin	36		X	25 mg. q.i.d.	2-4	excellent	+	—

* Superior to (+) Equal to (0) Inferior to (—)

Summary

Toclase (carbetapentane citrate), a new non-narcotic antitussive agent, with a selective ability to centrally depress the cough reflex was given to 44 patients of all ages who were suffering from coughing paroxyms of varying etiology (Tables 1, 2, 3).

Without exception there was excellent inhibition of the cough reflex and, in certain cases with an allergy, relief of the primary hypersensitivity symptomatology, such as wheezing in asthmatics. The local anesthetic action of Toclase afforded immediate and prolonged relief of pharyngeal discomfort.

The most remarkable feature noted throughout this study was the uniformly good patient acceptance of Toclase in its liquid dosage forms. All the patients, even the most neurotic, commented on the fine palatability of both Toclase syrup and Toclase expectorant compound. Further, no difficulties were encountered in administering liquid Toclase to children.

The side effects of Toclase were found to be minimal and of no serious import, except in one case. This patient developed a true drug rash which cleared only after cessation of medication.

In summary, it is concluded from the results of this clinical test that Toclase is an excellent antitussive agent which fulfills the criteria requisite for such a drug: i.e., it effectively depresses the cough reflex, is non-narcotic, is free of serious side effects, and is uniformly well accepted by patients.

References

1. Levis, S.; Preat, S.; and Moyersoons, F.: Pharmacological Study of a New Anti-Cough Remedy. From the Biological Research Laboratory of Union Chimique Belge, Brussels, Belgium.

2. DePoorter, D.: Clinical Tests on a New Cough Sedative. Bruxelles med., June 7, 1954.

3. Unpublished data in the files of the Medical Department of Pfizer Laboratories, Brooklyn, New York.

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Agammaglobulinemia is the name given to a new syndrome described as a clinical entity by Bruton in 1952. As the name clearly states, the typical alteration is the absence of the gamma globulin fraction in the human plasma. This definition being a rather exclusive one, it limits very greatly the incidence of the syndrome. Very absolute definitions, indeed, do not enjoy longevity in biological sciences and in medicine in particular; and it is quite possible that before long even this one may have to be changed to a less rigid one. Hypogammaglobulinemia would actually be a better definition of the syndrome.

It is impossible to exclude the presence of even small amounts of a substance as poorly known as gamma globulins from the plasma. The methods of assay are at the present time not sufficiently accurate. It would be better to speak of absence of "measurable amounts" of gamma globulins. This, we believe, is not merely a philosophical consideration, but one of a certain importance to the understanding of the entity, as it will later become apparent.

We decided, however, to retain the denomination of agammaglobulinemia because of the wide acceptance of the term in the literature, with the reservation that in this review will be included under the name of agammaglobulinemia only the cases in which no gamma globulins could be demonstrated by electrophoretic analysis of the plasma proteins, *before* attempts were made to raise the gamma globulin level with immunization procedures, or with exogenous administration of gamma globulin.

The following is a definition given by Prazad and Koza:[1]

1. History of recurrent bacterial infection
2. Absence of acquired antibodies
3. Lack of isohemoagglutinins
4. Extremely low to absent gamma globulins, although total serum proteins are within normal range
5. Failure of long-term antibiotic therapy to furnish protection
6. Response to protective injection of gamma globulin

We believe this definition to be incorrect in many respects and would like to modify it as follows:

1. Lack of measurable amounts of gamma globulin in the plasma
2. History of recurrent infections
3. Deficient or absent production of antibodies
4. Lack of isohemoagglutinins
5. Response to antibiotic therapy
6. Response to administration of adequate amounts of gamma globulin

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Agammaglobulinemia was first described in an eight-year-old boy by Bruton[1] and since then several other reports have appeared in the literature. Most of these case reports are, indeed, to be found in pediatric literature. The reason for our interest in the syndrome is not only due to the fact that recently some of the cases have been described in adults, but also because of the fact that due to successful management of the cases occurring in childhood and subsequent survival of these young patients, it will not be long before the pediatrician will hand them to the internist for further care. Besides, the disease is by no means a rare one. Since the first description a little over two years ago, some twenty-five cases have been reported; and, certainly, the number will rapidly increase in the future—especially if the physicians will be aware of the existence of the syndrome and take the necessary steps for its detection.

Case Reports: Bruton[1] in 1952 first described a case of agammaglobulinemia in an eight-year-old boy. This young patient had a long history of repeated infections since the age of three. The list included rubeola, herpes zoster, several episodes of pneumonia, varicella, five recurrences of otitis media, three of epidemic parotitis. Altogether, the boy had had clinical evidence of sepsis 18 times. Eight different types of pneumococci were isolated from blood cultures ten different times. All the bacterial infections responded promptly to penicillin and sulfonamide treatment, while prophylactic treatment with sulfadiazine in the dose of 1 gm. daily did not prevent recurrences.

It was thought that the patient could not produce antibodies against the pneumococci; antigens were prepared containing different types of pneumococci, but no specific antibodies could be demonstrated after their administration to the patient. This finding led to further immunological investigation. A Schick test was positive, although the patient had received diphtheria toxin series in infancy and booster doses at three years and again at six. A third and fourth booster dose failed to invert the Schick test. No antibodies were formed to typhoid vaccine and no complement fixing antibodies were present during an episode of epidemic parotitis.

Electrophoretic analysis of the serum gave completely negative results for gamma globulin. The total serum proteins and the A/G ratio were normal. 20 c.c. of immune human serum globulin (containing 3.2 gm. of gamma globulin) were injected subcutaneously. Six days following this injection, a concentration of gamma globulin equivalent to about 50% of normal, was found present in the serum. The gamma globulin slowly disappeared from the serum; and in approximately six weeks, no gamma globulin was present—the half life of administered gamma globulin having been of approximately 20 days. Accordingly, gamma globulin was administered in the same dose monthly; and without any other prophylactic measure, there was no further recurrence of sepsis.

In the same year, Bruton and others[2] described two other similar cases. The two patients were again boys, about eight years of age, with long history of pneumonias, pyoderma, sinusitis, pyogenic arthritis. One of them had hemophilus influenzae meningitis and the other meningococcal and pneumococcal

meningitis. The children failed to produce demonstrable amounts of specific antibodies after series of injections of diphtheria, pertussis, tetanus toxoid, pneumococcus polysaccharide, influenza virus, A and B vaccine. Total serum protein albumin and globulin concentrations were normal.

No gamma globulins were found at electrophoretic analysis, but minute amounts of gamma globulin could be detected with immunological methods. Examinations of the parents, one set of grandparents, and siblings revealed normal amounts of serum gamma globulin.

Janeway and others[3] in 1953 reported nine similar cases. At autopsy performed in one case, a low content of gamma globulin in the lymphoid tissue was found to be the only change. Connective tissue biopsy also revealed low gamma globulin content.

Later Keidan *et al.*[4] reported the case of a fatal reaction to vaccination. The procedure was performed on an eight-weeks old, apparently normal, girl and was followed by generalized vaccinia and death. Viraemia was demonstrated. No specific antibody could be demonstrated in the serum of the patient, except after transfusion with serum from recently immunized donor. Nine days following this transfusion, no demonstrable antibody activity was found present in the patient's serum.

750 mg. of gamma globulin were also administered, but no antigenic activity was found in the serum a few days later. Gamma globulins were found absent on electrophoretic analysis approximately 40 days following vaccination and seven days prior to exitus. At autopsy there was absence of inflammatory reaction in the skin and of lymphocytes in sections of the spleen and lymphnodes, while monocytes and plasma cells were present in abundance. There was no enlargement of the spleen.

It is interesting to note that eight cases of generalized vaccinia following vaccination had been previously reported with history strikingly similar, but since the syndrome of agammaglobulinemia had not been recognized at the time, no serum fractionation studies nor immunological studies are available. It is quite possible that these cases are unrecognized cases of agammaglobulinemia.

Moncke[5] described a case of agammaglobulinemia in a 16-year-old boy with pneumococcal meningitis. This patient had a long history of repeated infections, furunculosis, pneumonias, repeated otitis media, bronchitis. On paper electrophoresis no gamma globulin could be demonstrated in the plasma. Penicillin and sulfa drugs therapy controlled the infection. The administration of 0.3 gm. of gamma globulin daily for nine days kept the patient free of infection for two months, although no gamma globulin could be demonstrated in the serum with paper electrophoresis. At the end of the two-month period, the patient had otitis media.

Three more cases were described by Hyles *et al.*[2] in a five-month-old baby boy and in two nine-year-old boys—two of whom died. The usual history of repeated infections could be obtained. The response to antibiotic therapy was good, except in one patient, who died 42 hours after admission for pneumonia and lung abscesses. Two of these patients had lymphopenia at some time during observation.

Another case is described by Bound *et als.*[11] in a one-month-old boy who presented edema of legs and poor development. The plasma proteins were low and absence of gamma globulin was repeatedly demonstrated with electrophoretic determination. Although not subject to infection when first seen, this young patient had very severe bacterial infections later. Very interestingly, a sister of the patient had presented a similar clinical picture in her infancy and died after several repeated infections. Unfortunately no electrophoretic determinations are available in this case.

A number of other cases appear to have been discovered, although not yet published. Two such cases are reported by Good.[12] The history is typical: repeated infections, no demonstrable gamma globulin, no evidence of serum antibody, absence of isoagglutinins against heterologous blood groups, no production of circulating antibody following a variety of antigens.

Craig *et als.*[13] mention "children" found to be agammaglobulinemic; neither sex nor the precise number are given.

A few other cases are mentioned in discussions in the "Transactions of the Society for Pediatric Research" (one of the mentioned cases is said to be 79 years of age). It is to be expected that a very great number of cases of agammaglobulinemia will be published shortly. There is, furthermore, a great number of cases which are very suggestive of being true agammaglobulinemic states,[10] but which were, unfortunately, not proven with electrophoretic studies.

Long *et al.*[6] describe another case in a 29-year-old woman. The usual history of repeated infections was present. Antibody formation was absent, except for slight antibody formation against diphtheria, typhoid and paratyphoid vaccine.

Zinneman *et als.*[7] describe three other cases in adults:

1. A 29-year-old man with bronchiectasis and repeated pneumonias controlled by antibiotics.

2. A 37-year-old man with repeated pneumonias.

In both cases no gamma globulin could be found with electrophoretic analysis of the serum proteins. There was no antigenic response to typhoid-paratyphoid vaccine and the polysaccharide type I and II of Diplococcus pneumoniae. The first case responded very poorly to Brucella abortus antigen, while the second did not. The repeated infections could be controlled by antibiotics. Injection of pooled gamma globulin once monthly for six months protected the second patient from infection, while the first patient had two pneumonias while on gamma globulin treatment. Antibiotics promptly controlled the infections and prophylactic antibiotic treatment with penicillin or tetracycline seems to maintain these people free from infections.

3. The third case was that of a 30-year-old woman who had pneumonia 44 times in 11 years and pneumococcal meningitis three times. This patient also presented splenomegaly, which eventually led to splenectomy. Histological lesions similar to those found in Boek's sarcoid were found in the spleen.

Leukopenia was present before splenectomy, but normal W.B.C. counts were obtained after removal of the spleen. Gamma globulins were absent on elec-

trophoresis. No antibodies were formed to the typhoid, paratyphoid vaccine, Brucella abortus and the polysaccharides of Diplococcus pneumoniae type I and II. The patient's type being O, no agglutinins were found against type A and B cells, and injection of one c.c. of type AB blood failed to produce isohemoagglutinins. Plasma cells were absent in the spleen and lymph nodes.

Grant *et als.*[7] in England also report a case in a 17-year-old girl who in the preceding one and one-half years had seven pneumonias, several other febrile reactions, and cellulitis. This case presented two unusual features: 1) Leukopenia persisting even during an attack of pneumonia (her blood count never showed more than 4,000 W.B.C., and once during a pneumonia, the count was 2,000; the leukopenia affected polymorphs and lymphocytes equally); 2) splenomegaly.

The patient apparently had been in good health until 15 years of age, except for measles and whooping cough; after the age of 15, the patient had two more attacks of whooping cough.

There was slight hypoproteinemia, normal alpha 1 and alpha 2 globulins, and beta globulins. No gamma globulin could be demonstrated in the serum. The patient's blood belonged to Group O; no antiA antibodies were present. Anti-B antibodies were present.

Prasad *et als.*[14] describe the case of a thirty-year-old white female with long history of recurrent infections, splenomegaly, leukopenia. After splenectomy, the leukopenia disappeared. The spleen showed granulomatous formations which were not specific, although similar to the granulomata usually found in sarcoidosis. Complete absence of demonstrable gamma globulins and absence of response to immunization procedures were a feature in her case.

Agammaglobulinemia has been described in two cases of chronic lymphocytic leukemia,[17] in multiple myeloma,[17, 18] and in malignant lymphoma.[16] Of great interest is the fact that in this last case,[16] history of repeated infections preceded by about six months the enlargement of cervical nodes and by nine months the diagnosis of lymphoma. Also of interest is the absence of plasma cells in her bone marrow. Very recently in our wards one such case was described in a woman suffering from chronic lymphocytic leukemia.

Discussion: Having established in our definition that agammaglobulinemia is a state of absence of measurable amount of gamma globulin from the plasma, we shall now attempt to investigate the cause or the causes of such abnormality. We shall not discuss in detail the origin and formation of the gamma globulin, assuming, with the majority of authors, that the gamma globulins contain the greater part of the circulating antibodies and that one of the main sites of production is the plasma cells.

Let us consider some of the aspects of the syndrome as they appear in the light of the available work:

1. Agammaglobulinemia and Heredity: When agammaglobulinemia was first discovered, it was thought that the disease might be sex linked, since all the cases were found in males. It was also thought that the disease was congenital, because of the young age of the patients. Later, with the reports of absence of gamma globulin in the serum of females (the first to our knowledge, being that of Keiden *et als.*[4]) it appeared the disease was not limited to one sex.

The older age of some of the patients later reported, coupled with the fact that in many instances the onset of the typical history of repeated infections was preceded by a long period of apparently normal health, lead to the thought that the defect could be acquired in the course of life. Especially convincing to us in this respect is the finding of absence of gamma globulin in patients suffering from diseases such as lymphoma, multiple myeloma, chronic lymphatic leukemia. Although not at all explained, the finding of such an alteration in people who are victims of diseases which alter profoundly the normal status of the systems and organs which allegedly produce gamma globulin is not quite as surprising and incomprehensible.

2. Anatomical Changes in Agammaglobulinemia: Aside from the pathological findings due to the infectious processes, no specific anatomical change has been found to be typical of the disease. Many of the reports fail to show any pathological finding at all, while other authors have reported abnormalities in organs which are connected with antibody production. Of great interest, are the three cases described by Zinneman,[9], Grant,[8] and Prasad.[14] They are quite similar in many respects: the three patients were women in middle age; all had splenomegaly, leukopenia; in two cases, the spleen was removed and granulomata were observed formed of epithelioid cells, giant cells of the Langan's type and small areas of necrosis. In both cases, the diagnosis of sarcoidosis was considered, but not established. One of these patients was remarkable for absence of plasma cells from spleen and lymphnode biopsy. In both the cases of splenectomy, the leukopenia subsided after operation. The absence of plasma cells is of great interest, since these cells are thought to be the main source of gamma globulin under normal conditions and under stimulation. Other authors reported absence of plasma cells from spleen or lymphnodes. Arends[16] reports absence of plasma cells in his patient's marrow.

Good[12] also reports absence of plasma cells from lymphnodes and bone marrow in two agammaglobulinemic patients. He also studied the response of lymphnodes and bone marrow of these two individuals to antigenic stimulation, as compared to normal subjects. While normal individuals responded with a plasmacytosis, the patient's marrow and nodes showed persistent lack of plasma cells.

Craig et als.[13] also report anatomical changes in lymphnodes of agammaglobulinemic patients and remarkable absence of plasma cells.

Interestingly enough, Keidan *et al.*[4] reported absence of lymphocytes in spleen and lymphnodes in their case, while monocytes and plasma cells were present in abundance. The spleen was not enlarged at autopsy.

3. Chemical Changes in Agammaglobulinemia: The typical change in agammaglobulinemia is the lack of gamma globulin in the serum. The total proteins may be lowered, in some instances, especially in agammaglobulinemia found accompanying the syndrome of idiopatic hypoproteinemia.[11] In other cases, no abnormality in the plasma protein was concomitant. Still in other cases, different changes in the alpha 1 or alpha 2 or beta globulins, ranging from moderate increase to decrease, have been described, but without any typical pattern. Also typical is the

low level of antigens following immunogenic stimulation.

4. Etiology of Agammaglobulinemia: As with any condition of deficiency, the question that is always raised is whether the deficiency is due to a decreased production or an increased destruction of the normally produced substance. At present, the bulk of evidence is in favor of a decreased or altered production of gamma globulin, rather than an increased destruction, as the mechanism of production of agammaglobulinemia.

The rate of destruction of administered gamma globulin has been determined in a few cases and found to be comparable to the rate of destruction in the normal.[4, 5] In an attempt to determine the cause or causes of agammaglobulinemia, let us examine the conditions which have been found to be associated with hypogammaglobulinemia. These are several:

a. The nephrotic syndrome, in which deficiency of gamma globulin is usually associated with deficiency of serum albumen, as well shown by Squire.[19]

b. Poor nutrition.[20]

c. Infection.[21] Wyngaarden describes the case of a 3½-year-old Negro boy in whom a transient hypoproteinemia, marked hypogammaglobulinemia, edema, and weight gain followed an acute tonsillitis. Normal protein levels were again restored 10 weeks following the onset of the disease.

d. Lymphomas.[16]

e. Aside from these four situations, there is another group of individuals with marked hypogammaglobulinemia which accompanies a poorly defined syndrome of so-called idiopatic hypoproteinemia.[22, 23] This is thought to be a congenital defect and has been described in a small number of children. It usually manifests itself clinically as an edematous state accompanied by impairment in growth and development.

Schick and Greenbaum[24] described an 11-year-old girl who had recurrent edema from birth; the serum albumin and globulin, and especially the gamma globulin, were decreased.

Hertzog and Faust[25] reported a boy with the same syndrome.

Homburger and Peterman[26] described a syndrome of idiopatic familial dysproteinemia with abnormalities in the electrophoretic pattern of the plasma, with or without hypoproteinemia. Edema was present without a decrease in protein normally considered sufficient to produce edema. The mother of certain of the cases had five stillborn, edematous fetuses, although no Rh phenomenon was involved.

f. A physiologic decrease in gamma globulin also occurs in the infant soon after birth. Rather low levels are reached before the restoration of normal levels is accomplished.[27]

It is possible that agammaglobulinemia may represent an exaggeration of one or more of these conditions. For instance, it is conceivable that a very severe infection may overwhelm the productive power of the gamma globulin-forming organs, whichever they may be, and induce transitory or permanent paralysis of these organs—especially if this infective agent happens to attack the host while in a state of hypogammaglobulinemia physiological or pathological.

It is interesting to note that the state of acquired "immunological paralysis" was obtained experimentally by Felton[28] in mice with the injection of large doses of pneumococcal polysaccharide.

It is possible to ascribe at least some of the cases to a congenital defect, similar to hemophilia, or the more recently described congenital afibrinogenemia. Some of the cases appear to be secondary to alteration in the blood-forming organs, such as the cases following leukemia, multiple myeloma, lymphoma. The finding of absence of gamma globulins in the case of multiple myeloma is quite surprising, but not incomprehensible if we consider the profound alteration undergone by the plasma cells.

And of great interest in this regard, is the description by Janeway[29] of a syndrome clinically similar to agammaglobulinemia, i. e. characterized by repeated infection but with an elevation of serum gamma globulins. It is to be presumed that the gamma globulins present in this case are grossly abnormal and presumably unable to perform the same functions as the normal gamma globulins.

A similar report comes from Lawson *et al.*[18] who tested the anti-body content of the blood on nine patients with multiple myeloma. They found a marked decrease or total absence of the antigenic activity in the plasma of such patients. The gamma globulin content of the plasma ranged from marked increase to absence in one case. Very probably the immunologic abnormalities are due to abnormal function of the malignant plasma cells and consequent production of abnormal proteins, and, in particular, anti-body proteins.

5. Therapy of Agammaglobulinemia: It appears that at the present time the therapy consists of the use of appropriate antibiotics during acute attacks. Prophylactic treatment with antibiotics is also possible and, perhaps, the best available. Administration of exogenous gamma globulins has also been followed by good response. The experience has been very limited, but it appears that injections at monthly intervals are sufficient to protect agammaglobulinemic patients from recurrent infections.

Bibliography

1. Bruton, O. C.: Agammaglobulinemia, Pediatrics, 9:722 1952.

2. Bruton, O. C., Apt, L., Gitlin, D., Janeway, C. A.: Absence of Serum Gamma Globulin, Am. J. Dis. Child. 84:632 1952.

3. Janeway, C. A., Apt, L., Gitlin, D.: Agammaglobulinemia, Tr. A. Am. Physicians, 66:200 1953.

4. Kaldan, S. E., McCarthy, E., Haworth, J. C.: Fatal Generalized Vaccinia with Failure of Antibody Production and Absence of Serum Gamma Globulin, Arch. Dis. Childhood, 28:110 1953.

5. Moneke, C.: Schweiz. Med. Wchnshr. 84:1033 1954.

6. Long, N., Schattler, G., Wildack, R.: Klin. Wchnshr., 32:856 1954.

7. Hayles, A. B., Stickler, G. B., McKenzie, B. F.: Agammaglobulinemia, Pediatrics, 14:499 1954.

8. Grant, G. H., Wallace, W. D.: Agammaglobulinemia, Lancet, Vol. 2, 671 1954.

9. Zinneman, H. H., Hall, W. H., Heller, B. I.: Acquired Agammaglobulinemia, J.A.M.A., 156: 1390 1954.

10. Barbero, G. J., Gray, A., McNair Scott, T. F., Kempe, C. H.: Vaccinia Gangrenosa Treated with Hyperimmune Vaccinia Gamma Globulins, Am. J. Dis. Child., 88:395 1954.

11. Bound, J. P., Hackett, W. R.: Idiopatic Hypoproteinemia, Arch. Dis. Child., 28:104 1953.

12. Good, R. A.: Agammaglobulinemia, Tr. Soc. Ped. Res., Am. J. Dis. Child., 88:625 1954.

13. Craig, J. M., Gitlin, D., Jewett, T. C.: Tr. Soc. Ped. Res., Am. J. Dis. Child, 88:626 1954.

14. Prasad, A. S., Koza, D. W.: Agammaglobulinemia, Annals of Int. Med., 41:629 1954.

15. Brenn, T. H., Morton, M. E.: Agammaglobulinemia, V. A. Annual Med. Res. Conf., Memphis, Tenn., Dec. 1953, cited by*.

16. Arends, T., Conrad, E. V., Rundles, R. W.: Serum Proteins in Hodgkin's Disease and

Malignant Lymphoma. Am. J. Med. 16:833 1954.
17. Snapper, I., Turner, L. B., Moscowitz, H. L.: Multiple Myeloma. N. Y. Grune Stratton, 1953 page 83, cited by.*
18. Lawson, H. A., Stuart, C. A., Faull, A. M., Phillips, A. M., Phillips, R. W.: Antibody Content of the Blood in Patients with Multiple Myeloma. New Eng. J. Med., 252:13 1955.
19. Squire, J. R.: Brit. Med. J., 2:1939 1953.
20. Krebs, E. J.: Journal Lab. Clin. Med., 31:85 1946.
21. Wyngaarden, J. B., Crawford, J. D., Chamberlin, H. R., Lever, W. F.: Pediatrics, 9:729 1952.
22. Thompson, W. H., McQuarrie, I., Bell, E. T.: Edema and Hypogenesis of Serum Proteins. J. Ped. 9:604 1936.
23. Rytand, D. A.: Edema with Hypoproteinemia. Arch. Int. Med. 69:251 1942.
24. Shick, B., Greenbaum, J. W.: Edema with Hypoproteinemia. J. Ped. 27:241 1945.
25. Hertzog, F. V., Faust, O. A.: J. Ped. 16:641 1950.
26. Homburger, F., Peterman, M. L.: Blood, 4:1085 1949.
27. Orlandini, O., Sass-Kortsack, A., Ebbs, J. H.: Serum Gamma Globulin Levels in Infancy. Am. J. Dis. Child., 84:632 1952.
28. Felton, L. D.: J. Immunology, 61:107 1949.
29. Janeway, C. A.: Hypergammaglobulinemia. Am. J. Dis. Child. Sept. 1954.
30. Zinneman, H. H., Hall, W. H.: Recurrent Pneumonia in Multiple Myeloma, cited by.*
31. Brem, T. H., Morton, M. E.: Agammaglobulinemia, cited by.*

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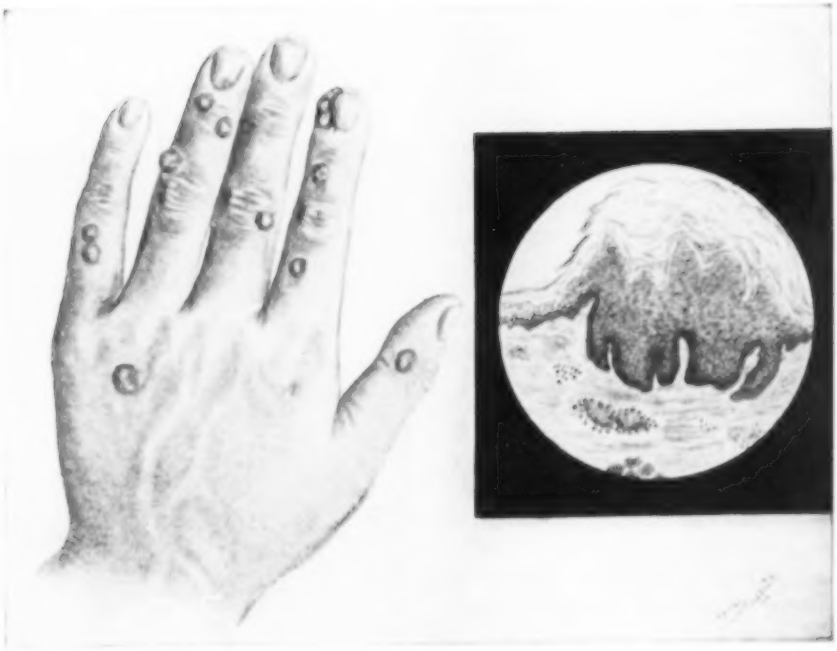

Verrucae vulgaris on the hand and fingers.

Microscopic appearance of verruca vulgaris.

Foam Rubber Compression In the Treatment of Stasis Ulcers

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Localized compression by sponges has long been recognized as an important implement in the treatment of the post-phlebitic pathology. It increases the effect of circular compression bandages, especially in the space anterior to the Achilles tendon, where the compressive effect of circular elastic bandages becomes lost during walking.

Originally, marine sponges were used. Cotton, gauze or mechanic waste were recommended. All this material has been replaced later on by foam rubber. It is available in different shades of elasticity, density and porosity. For the purpose of efficient compression, the property of the material must be such that on one hand no pressure damage is caused, and on the other hand, the elasticity must be sufficient to permit effective compression.

K. Sigg[1] who has treated thousands of ulcers conservatively, chose a product of medium elasticity and porosity. He designed three patterns: (Fig. 1)

1. A kidney shaped pad, suitable for application to the ankle: 5 inches x 2¾ inches x ¾ inches.
2. A rectangular pad: 6¾ inches x 5 inches x ¾ inches.
3. A rectangular pad of larger size: 10 inches x 8 inches x ½ inch.

The corners of all 3 sponges are rounded and the edges bevelled. The sponges can be sterilized.

It is not advisable to place the sponge directly over the ulcer. The latter one is covered with a gauze compress, to which ointment or powder may be applied. The sponge is encased in an elastic bandage (Fig. 2). It is important that the heel is completely enclosed in the bandage to avoid localized edema.

The large pad can be used for compression therapy of acute, superficial

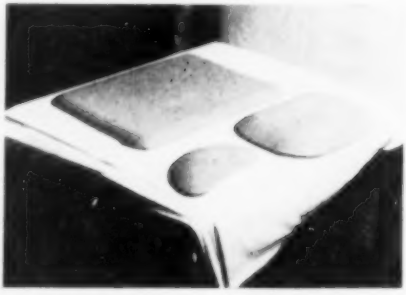


Fig. 1. Compression sponges of different shapes.

phlebitis or large areas of stasis pathology. In this case, it may be applied to the intact skin, unless there are reasons to fear allergic reactions.

Elimination of large venous sinuses by sponge rubber compression is the main reason for the therapeutic effect. These venous lakes surrounding ulcerations impede the exchange of metabolites, oxygen and water. Another important effect of compression bandages is the avoidance of stasis edema which in many cases is the cause of therapeutic failures.

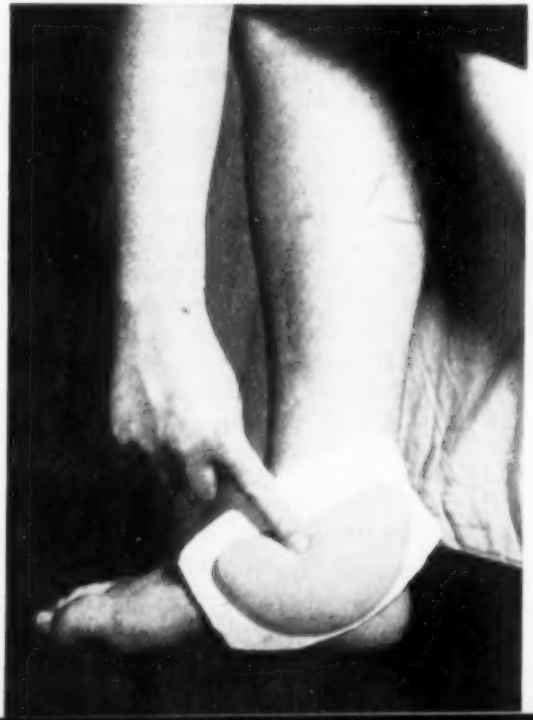
Following cases demonstrate the importance of adequate sponge rubber compression therapy:

58-year-old white female, complains of painful hyperplastic cellulitis (7.5 x 4 cm) of the left lower leg. Serology, urinalysis negative. At the first visit the patient was advised to use an elastic

2B

Figs. 2A&B. Placement of gauze and sponge over ulcer and application of elastic bandage. Courtesy of Dr. K. Sigg: Angiology 3:255, 1952.

2A



bandage plus a 1 inch thick foam rubber pad. Three weeks later no changes were noted, and the patient was advised to undergo surgery. Since she refused, a trial with the described smaller rectangular pad (6¾ inches x 5¾ inches) plus elastic bandages enwrapping the left foot, heel and lower leg was made. At her next visit 5 weeks later, the infiltration had almost completely disappeared.

62-year-old white female, suffering from stasis cellulitis with multiple ulcerations of her lower leg of 10 weeks duration. The size of the affected area was 15 cm x 6 cm. There were nine ulcera-

The sponges were obtained through Medical Fabrics, Inc., Paterson 1, New Jersey.

tions covered with purulent membranes ranging from ½ x ½ cm to 1.5 to 1 cm in size. Chloramphenicol powder was applied to the ulcerations, the whole area covered with Lassar's paste, and an elastic bandage wrapped around the foot and leg. After 2 weeks the ulcerations appeared clean, granulations started to grow, but the cellulitis became progressive and had a more acute appearance at the margins. Systemic administration of antibiotics was badly tolerated. A large rectangular foam rubber pad (10 inches x 8 inches) was applied over a gauze pad, covering the diseased area, a 3" elastic bandage wrapped around foot, heel and ankle, and a 4" elastic bandage around the lower leg from the ankle up to the knee. There was cessation of pain after 24 hours. One week later the area became pale and soft. The ulcerations were healed after 3 weeks. After 4 months the patient was allowed to omit the bandages.

Reference

1. Sigg, K.: The treatment of varicosities and accompanying complications. Angiology 3:255, 1952.

81 West Main Street

New Resident Physician Journal

Resident physicians are probably the last remaining group of physicians who have had no special journal of their own. Yet the resident has a great many problems which differ materially from those of either the practicing specialist or the intern.

To fill this void in medical literature a new journal, RESIDENT PHYSICIAN, makes its bow with the September 1955 issue. Its Editor-in-Chief, Perrin H. Long, M.D., will be assisted by a distinguished Board of Editors from leading medical schools and hospital centers.

The editorial content of RESIDENT PHYSICIAN, consists of original articles geared especially to residents' educational, economic and personal problems within and outside the hospital. Its main editorial aim is to make the resident a better house officer, and generally provide him with the economic information that he is neither taught nor given in his specialty journals.

Some of the articles scheduled for early publication are:

- Is Private Ward Service Necessary?
- How to Manage a Ward
- Fellowships for Residents
- Tips or No Tips
- Preparing for State and Specialty Board Examinations
- Buying a Home and Office
- Fee Schedules
- How to Build a Practice
- Pyramidal Residency vs. Columnar Residency
- How to Gain Fullest Cooperation from the Hospital Administration.

Nutritional Fatty Liver; "Kwashiorkor"

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Nutrition, until very recently, has been one of the most neglected stepchildren of medical science. Discoveries in the field of nutrition have been for long only byproducts of unrelated or only indirectly related experimental investigations. Only in the last decade has the field of nutrition and its vast pathophysiological applications aroused vivid interest resulting in a spurt of active clinical and biochemical investigation. In this review the attempt is made to discuss the influence of nutritional deficiencies upon non-physiologic accumulation of fat in the parenchyma of the liver, the suspected mechanisms involved in its deposition and the clinical picture in man, Kwashiorkor.

Hepatic parenchyma may be a victim of any injurious agent, be it toxin, anoxia, anemia or dietary deficiency. Among the structural components of the liver in addition to the supporting structures and vascular and lymphatic systems three differentiated and functionally active tissues may be involved:
A. Kupfer-cells, which are a part of the almost ubiquitous reticulo-endothelial system, are the least differentiated.
B. The cells of the biliary tracts are less specific for the liver but still highly differentiated and
C. The parenchymal cell, which is entirely characteristic of the liver and most differentiated. The latter is subject to the most severe injury and may often be the only site of injury, while other structures may remain intact. In chronic hepatic injuries the fibrous-connective tissue takes part in the tissue response, proliferating abnormally intertwined in the damaged parenchymatous structure. The advanced stages of chronic injury resemble each other very closely no matter what the noxious agent was. With disregard for the importance of the dynamic sequence of pathophysiologic processes and the multitude of injurious agents that may be involved in their causation, the end stage, cirrhosis, is considered a disease entity. Himsworth stated "that retention of that view is one of the main obstacles to a better understanding of liver disease and, if this be so, no better contribution could be made to progress in this field, than to relinquish, both in clinical medicine and pathology, the use of the term 'cirrhosis' which not only misleads by implying an entity, whose existence is

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doubtful, but has become so worn and defaced by loose usage as to have lost all precision." The recent experimental work in nutritional liver disease and detailed studies of Kwashiorkor in children of the s.c. backward areas of the world has stimulated this series of two reviews which include nutritional fatty liver and liver necrosis; the latter will be presented shortly by Dr. J. Gardner.

Relationship of fatty liver and liver necrosis These two distinct pathological pictures have been produced experimentally by highly purified, selective diets and their distinct nature as two separate deficiency syndromes has been definitely demonstrated in 1942 by Daft, Sebrell and Lillie and confirmed subsequently by other investigators. It has become clear through experimental and

Table 1

	Liver Necrosis	Fatty Liver, Cirrhosis
Disease process	Degenerative metabolic change of the liver parenchyma leading to sudden, acute attack of massive necrosis	fatty metamorphosis of liver with a slowly developing fibrosis cirrhosis
	No fatty infiltration	No (massive) necrosis
	No fibrosis	
Residual signs	postnecrotic scarring	cirrhosis
Protective factors:		
Cystine*	protects	enhances
Vitamin E	protects	without effect
Factor 3	protects	not known
Choline	enhances	protects
Betaine	enhances	protects
Methyl group precursors	enhances	protects
Vitamin B_{12}	enhances	protects
Folic acid/citrovorum factor	enhances	protects

*Methionine has been shown to be protective against fatty liver and cirrhosis; it contains a labile methyl group.

It is also slightly protective in dietary necrotic liver degeneration, since it is partly transformed into cystine in intermediary metabolism.

human studies that both syndromes are a result of a complex nutritional deficiency rather than lack of one single factor. Different causative and protective factors have been recognized and their significances as well as their mode of action has been argued. The following table (Klaus Schwarz) summarizes the situation as based on experimental studies.

The dietary factors which protect against human fatty liver and cirrhosis have not been elucidated as yet. As it is apparent from the above table, not only do the factors producing these two distinct lesions differ, but some that prevent one type of lesion may enhance the other and vice versa. It should be noted that there are differences in reaction of various species to these dietary factors. Hence one should not expect the human to respond exactly like the rat does.

After a period of confusion that followed the work of Daft, Sebrell and Lillie and which was characterized by reports incriminating all and every dietary factor for liver injury, save carbohydrates, Himsworth and Glynn confirmed the existance of two kinds of experimental dietary deficiency syndromes:

1. Massive necrosis followed in survivors by massive postnecrotic scarring and

2. Insidiously developing diffuse hepatic fibrosis.

Both of these distinct nutritional injuries lead to fibrotic changes in the liver but the types differ structurally in each and to only one is necrosis necessarily antecedent. This does not exclude the possibility of development of some necrotic cells in the course of cirrhosis. Many observers have reported their occurrence. However it is generally agreed upon, that massive necrosis is definitely not a part of the process. Diffuse fibrosis has never been reported reliably as a result of massive dietary necrosis. Daft states that when the two pictures, cirrhosis and necrosis, occur together they appear to be essentially unrelated to each other, the hemorrhage and necrosis being superimposed upon any phase of developing cirrhosis. Daft emphasizes the fact that experimental development of both lesions depends to a large extent on the level of protein in the diet. It is beyond the scope of this review to discuss in detail the biochemical relations and difference of these two syndromes.

It should be noted that the term massive necrosis (equivalent to the term used in older literature of acute yellow atrophy) refers to a necrotizing process involving the entire lobule, every parenchymal cell in it. This has to be distinguished from zonal necrosis involving one part of the lobule only. The two terms, zonal and massive, apply only to the state within one lobule, and does not in any way imply the extent of involvement of the liver as a whole.

Sequence of events and morphology of fatty liver and diffuse hepatic fibrosis in experimental animals Diffuse fibrosis develops in livers which are the seat of heavy and prolonged infiltration—experimentally such infiltration is usually due to presence of neutral fat. Himsworth suggests the sequence of events that occurs in animals on experimental diets:

1. In the first few months during which the animal gains weight, there is presence of neutral fat in the parenchyma with no other changes.

2. Later, although there are no macroscopic changes other than fatty liver, special stains reveal thickening of reticu-

lin fibers in the region of the portal tracts or central veins. These fibers eventually grow towards each other to join in formation of a fine fibrous network throughout the entire parenchyma, isolating and intersecting the single lobules.

3. Subsequently bands of reticulin thicken and mature, taking stains for fibrous tissue. Fat diminishes in the organ and its stain changes to bronze.

4. Eventually the fibrous tissue contracts, the encircled parenchyma proliferates and as a result the surface of the organ becomes finely granular. Histologically the lobular architecture is markedly disturbed, uniformly throughout the entire organ.

It is impossible to find one normal portal tract or central vein. The bile ducts have grown along the fibrous bands so that not only portal veins and hepatic arteries but central veins also have now their accompanying bile ducts. Encircled lobules concentrically hypertrophying form nodules devoid of normal vascular pattern: excentric atrophy of other lobules leads to occlusion of the remaining veins by the fibrous tissue. The parenchyma shows less fat and minor degenerative changes. This is a classical picture of portal cirrhosis or diffuse hepatic fibrosis which must be differentiated from post necrotic fibrosis on the basis of the following criteria:

1. The development is insidious, not sudden;
2. Frank necrosis does not occur in any stage;
3. The process is uniform and when the lesion is established every lobule is affected and no normal lobular structure can be found.

Hartroft described an interesting concept based on his histologic observation in development of fatty liver cirrhosis in rats fed choline free diet. He observed that after a few hours of low choline diet fat is deposited within the liver cells and seems to be localized chiefly in the center of the lobules rather than portal regions. Only in the later stages fat droplets can be demonstrated in the portal regions. Hartroft designated this early stage of the dietary fat deposition within the cell as lipohepatosis, a term which eliminates the misleading implications of terms such as fatty change, infiltration or degeneration. The phase of extracellular lipohepatosis follows when choline deficient diet is being continued. This stage results from the excessive intracellular fat accumulation, which may reach the point of rupturing the cell. The fat globules thus escape the cellular limit and by enlarging it compress the adjacent segment of the neighboring cell membranes. Coalescence of these fat globules surrounded by crescentic membranes of the cytoplasm of the torn cells leads to the formation of epithelial fat-laden cysts. Many of these fatty cysts may coalesce by expansion. Eventually the intracystic fat may escape through the established communications with sinusoids and bile ductules. Concomitantly with the rupture of cysts trabeculate begin to form and Hartroft believes that they result from condensation of the parenchymal and stromal remnant of the ruptured fatty cysts. The rupture of large cysts which results in the escape of fat leads eventually to formation of a fibrotic residuum out of their surrounding structures. Consequently a fibrotic trabecular network forms connecting adjacent centrolobular regions which represents an early stage of experimental dietary cirrhosis in animals. The term portal

cirrhosis is acceptable only from a purely descriptive standpoint in this stage but it should be realized that the sites of fibrosis are actually non-portal with reference to blood supply. Hartroft also believes that in alcoholic portal cirrhosis "the parenchyma around terminal portal venules is usually quite free of fibrotic venules lesions, although the large conducting veins frequently are surrounded by pathological amounts of fibrosis. This suggests that the distribution of trabeculae in alcoholic cirrhosis in man is also periportal in a geographic sense only and that in this respect as well as perhaps in others dietary cirrhosis in choline deficient rats is the morphologic counterpart of that found in alcoholic man. In advanced stages of choline deficient diet after 4-5 months hyperplasia characterizes liver architecture. Nodules of compensatory proliferation of parenchyma and mitotic figures are the striking feature. Rarely significant fatty deposition is seen in this stage in spite of continuation of low choline diet.

As it will be apparent from the subsequent discussion the concept presented by Hartroft is by no means universally accepted.

Relationship of fatty infiltration to liver fibrosis in malnourished man and in experimental animals

Studying the adult African population by means of liver biopsies and in autopsy material Gillman and Gilbert concluded that there is no concrete basis for claiming the existence of a direct causal relationship between fatty infiltration and fibrosis. Their conclusion is based on the following facts:

1. The fatty change in the livers in infant and adult Africans is of relatively acute onset,

2. After the acute episode the fat usually disappears from the liver,

3. Sampling of livers from general population of Africans at all ages affords no evidence of a persistent and progressive fatty change,

4. Evidence of fibrosis in general population of Africans cannot be correlated positively with hepatic steatosis.

They also supply some experimental evidence that animals having an extensive fatty change in the liver failed to show any evidence of fibrosis. They agree with the observation that the dietary deficiency is the causative factor in fibrosis but believe that steatosis and fibrosis result from two separate processes not necessarily related to each other and that fibrosis in malnourished Africans does not occur through the mechanism of fatty infiltration. There may be an indirect relationship between these two processes, fatty degeneration being associated with varying degree of catabolism which in turn may stimulate the reticulo-endothelial system to production of fibrosis over a long period of time. Davies concurs with the concept that fatty change and fibrosis are not causally related. He believes that they are in a chronologic relationship to each other rather than a causal one. As fat leaves the cells fibrosis becomes more apparent; although fibrosis may start with the fatty infiltration it may occur without preceding fatty deposition. Waterlow described occurrence of fibrosis in West Africa without apparent fatty infiltration. Others observed very severe fatty infiltration with minimal fibrosis and visa versa. Davies believes that the evidence would point to two separate etiological factors, one causing fatty metamorphosis the other fibrogenesis. The massive fatty infiltration, he observed in malnourished children, is not

very common in adults and there is no evidence to suggest that the cases of Laennec's cirrhosis seen in Africans are direct consequence of a long and continued period of fatty infiltration in adolescence. Pleading ignorance as to the definitive knowledge of the answer to this problem he is inclined to believe that the high insidence of cirrhosis is due to infectious hepatitis rather than a sequence of fatty metamorphosis. On the other hand Hartroft cites convincing experimental evidence and observations in cirrhotic men pointing strongly to a direct cause and effect relationship between what he calls lipohepatosis and cirrhosis.

Glynn, Himsworth and Lindan are of the opinion that the experimentally produced cirrhosis is almost certainly a sequence which occurs in human beings and which is a direct consequence of a prolonged fatty infiltration of the liver. Whether it is an invariable sequence in the evolution of diffuse fibrosis, Glynn is not certain. He states however definitively that in parts of the world where severe malnutrition prevails fatty infiltration is a stage in evolution of diffuse hepatic fibrosis. This group is inclined to the view that the cirrhosis is a result of a circulatory insufficiency through the sinusoids of the liver due to their compression by massively distended liver cells infiltrated by fat. Dubin disagreeing with the view expressed by Hartroft stated that on the basis of a study of 400 cases of portal cirrhosis (s.c. nutritional or alcoholic cirrhosis) no fatty cysts have been observed with rare exceptions and he expressed the opinion that fatty metamorphosis in itself does not lead to hepatic necrosis or cirrhosis. Cases of fatty liver studied by liver biopsies over a period of 2 or 3 years failed to show significant portal fibrosis without affecting appreciably the degree of portal cirrhosis. He believes that, the prime lesion in human portal cirrhosis is necrosis. The presence of fat is marely a parallel phenomenon. Popper assumes a compromising position believing that there are various pathways through which fatty liver may go into cirrhosis. He agrees with the concept of fatty cysts provided that large amounts of fat are present and the concept of necrotizing and inflammatory process complicating fatty liver. Citing Dr. Hans Elias' studies based on three dimensional reconstruction and geometrical analysis, he believes that stress within the parenchyma "exerted from the vicinity of regeneratory ordinarily fat free liver cell plates, usually several cells thick and the fat containing one cell thick plates" is the most important pathway. "This stress produces planes of breakage in which fibers develop to form a straight septum, subdividing the lobule. In human fatty livers, where periods of nutritional disturbance alternate with at least partial recovery, these stress planes probably develop more readily." Popper concludes "that the degree of participation of the different pathways varies in the individual cases. This accounts for the polymorphic picture seen in the development of cirrhosis from the fatty liver in man."

One could cite these differing views with their more or less convincing evidences but it is already apparent that at this stage no conclusive answer to this very important question is available.

Metabolic aspects of fatty metamorphosis and cirrhosis The important role of the liver in fat metabolism has long been recognized. The modern isotope technics have proved this fact.

The liver can be regarded as a way station in the course of lipids from the fat depots or tissue cells. Depot fats are brought to the liver for the purpose of desaturation of fatty acids. The desaturation enables an easier oxidation of fatty acids by tissue cells. The liver is also able to perform the reverse process of saturating the ingested unsaturated fatty acids. This process may be important when dietary fats are chiefly composed of vegetable oils. Liver is the main source of phospholipids.

Most of the body cells are unable to utilize neutral fat, it has to be supplied for oxidation in form of phospholipids. In this process lecithins and various cephalins participate. Normally the liver contains about 5% of lipids most of it in form of neutral fat and phospholipids in equal proportions. Some hold the view that phospholipids are apparently important in direct removal of neutral fat from the liver back to the adipose tissue. Anything that interferes with the rapid turnover of phospholipids in the liver interferes with the transit of fat through this organ and thus producing fatty infiltration. Lipids may make up as much as 40% of the liver weight in severely fatty livers.

In starving animals, after a short period for depletion of reserves of glycogen, the reserves of fat are called upon. Large amounts of fat then appear in the liver. This seems to represent the first step in its metabolic breakdown. The transport of fat according to Bloor proceeds from depots in form of phospholipids and cholesterol esters of fatty acids. Both of these types of compounds are more soluble in plasma than is neutral fat. Studies with isotopic acetic acid have shown that cholesterol is synthesized from acetic acid by the liver, intestinal mucosa, skin and other tissues. The bulk of esterification of cholesterol takes place in the liver. Phospholipids include 4 groups, Lecithins, Cephalins, Plasmalogens and Sphyngomyelins. The first two seem to be the most important ones in fat transport. Lecithins contain in addition to glycerol and fatty acids phosphoric acid and choline. In cephalins ethanolamine replaces choline.

Lipotropic agents of which choline is the outstanding factor have been shown, in experimental animals, to protect the liver from developing fatty infiltration. The term lipotropic designates substances which decrease the rate of deposition and accelerate the rate of removal of excess fat and was so defined by Best, Huntsman and Ridout. The active principle is a component of the diet. The term is not applicable to changes in lipid concentration in blood or generally in the body. Best and Ass. express a regret that they extended the definition to include "prevention of renal lesion and cirrhosis". Outside of its lipotropic action choline has an effect on animal growth which may be mediated through its lipotropic action and antiperotic action in preventing renal hemorrhagic syndrome. Best states that choline's curative effect on fatty, cirrhotic liver also involves the reticular substance which proliferates secondary to deposition of fat. He is not certain however whether this is a part of its lipotropic effect. It is beyond the scope of this paper to discuss in detail many nonlipotropic effects of choline.

Besides choline, betaine, methionine and under some conditions vitamin B_{12} and possibly inositol protect rats and other animals from fatty infiltration.

Lipotropic activity of liver extract in rats on high-fat diets has been demonstrated and evidence seems to indicate that factors other than choline markedly influence liver fat content. Also marked lipotropic effect of hog stomach (ventriculin) and minimal effect of brewer's yeast have been demonstrated in experimental animals. Folic acid in combination with choline and B_{12} as well as citrovorum factor have been found to exert also lipotropic activity. Other substances not in themselves lipotropic may exert lipotropic effect or potentiate it. This may apply to antibiotics (aureomycin). Before reviewing the various views on the mechanism of their action it would be of interest to turn to text books of biochemistry to understand the basic reactions in which the crucial factor, the labile methyl, is involved.

Methionine contains a methyl group. This essential aminoacid readily donates its terminal methyl group for methylation of various compounds. In addition to utilisation of the methyl group in the intact form there is evidence based on experiments with methionine containing labeled methyl carbon that this methyl group is also oxidized. In the rat one-fourth of the labeled methyl carbon appears in the expired CO_2 during the first day and about one half of the labeled carbon is excreted in the urine, feces or respiratory CO_2 in two days. Methyl carbon may also be used to produce formic acid or formaldehyde, which conjugates with glycine in the synthesis of serine. Glycine reacting with serine produces ethanolamine which is an important component of phospholipids. The demethylation of methionine either for transmethylation or oxidation of the methyl group produces homocysteine. The latter together with a source of labile methyl can be used to replace methionine in the diet. The animal organism has some ability to synthesize methyl groups, and vitamin B_{12} and folic acid are involved both in the synthesis and utilization of these labile methyl groups. This fact is supported by the observation that while rats 30 days old or older can grow on a diet free of all methyl donors if vitamin B_{12} and homocysteine are present, poor growth is obtained on a diet containing ample methionine but free of vitamin B_{12}. Methionine content of protein because of its labile methyl group may be responsible for the lipotropic effect of protein.

Choline contains three methyl groups. Choline in its ready form apparently need not be supplied with the diet since it may be synthesized according to the requirements. The methyl groups may be supplied by methionine.

Glycine $\xrightarrow[\text{Reduced}]{}$ Ethanolamine

Serine $\xrightarrow[\text{Decarboxylated}]{}$ Ethanolamine

Ethanolamine plus methyl groups from Methionine Choline

Choline may also be a methyl donor. Betaine is another important methyl donor. The formation of choline by methylation is a reversible reaction, in which choline is oxidized to betaine. This oxidation process is mediated by the enzyme, choline oxidase. Labile methyl groups may be lost not only by transfer to other compounds which are then excreted; they may also be destroyed by oxidation. However, the animal organism has some ability to synthesize methyl groups. Vitamin B_{12} and folic acid are both involved in the

synthesis and utilization of methyl groups. Diversion of methyl groups from methionine for other reactions may lead to production of fatty liver if the dietary supply of choline is inadequate.

Drill stpdied the effectiveness of Ventriculin, liver extract and B_{12} on prevention of fatty liver found them effective either alone or in combination. Also yeast extract offered protection in animals fed low protein diet. Drill concludes that the effects obtained by administration of these agents can not be explained on the basis of their choline content. Shaefer and Ass. demonstrated choline sparing effect in lipotropic studies. Drill failed to confirm it. However, this question is not settled as yet. Vitamin B_{12} and the other factors mentioned may be either altering the rate of synthesis of the labile methyl groups or the process of transmethylation, but the exact mechanism is unknown. Diet deficient in B_{12} interferes with the ability of the liver to convert betaine and homocystine to methionine or choline and homocystine to methionine. Jukes, Stockstad and Broquist observed that Vitamin B_{12} was necessary for methylation of homocystine to obtain growth in chicks fed a methionine deficient diet. This action depends on the amount of methyl group available. Choline alone will prevent renal lesions when added to diets deficient in choline and methionine but will not increase body weight significantly. However, supplement of B_{12} in presence of choline will permit an adequate gain in weight. This indicated that the synthesis of methionine from homocystine was facilitated. When however the amount of methyl groups was limited by a further reduction in choline intake both B_{12} and folacin were needed for adequate growth. Folic acid deficiency was also found to interfere with methylation of homocystine. Need for both folic acid and B_{12} has been demonstrated. Shaefer and Ass. have demonstrated that to prevent renal lesions and fatty livers and promote growth in weanling rats fed basal diet with homocystine, betaine and aminoethanol the addition of B_{12} is necessary. Addition of B_{12} plus folic acid was necessary if betaine and aminoethanol are given in a lesser amount. It should be noted that aminopterin which is the folic acid antagonist inhibits choline oxidase activity, betaine aldehyde oxidase and aerobic and anaerobic transmethylation to homocystine. Thus folic acid plays a part in the conversion of choline or betaine aldehyde to the actual methyl donor betaine, and its transmethylation to homocystine. Stekol and Ass. have found that folic acid deficiency in adult rats reduces the capacity to utilize glycine or serine for production of choline. Gyorgy and Ass. reported that liver extract may enhance the effect of casein or methionine in treatment of experimental cirrhosis. Popper found that B_{12} concentrate in normal diets will inhibit fatty changes and depletion of ribonucleic acid in rats receiving a single injection of carbon tetrachloride. It is useless if intoxication continues. Aureomycin may exert a sparing effect on B_{12} as measured by growth response in rats and chicks. Vitamin B_{12} and/or aureomycin will counteract the effect of cortisone on the growth in rats. Inositol and aureomycin when added to combinations of folic acid, choline and B_{12} with citrovorum factor did not increase their lipotropic activity. Schwartz stated that in preliminary tests he found that

substances which are sources of methyl groups and substances like B_{12} and citrovorum factor which enhance production of dietary necrosis protect from development of fatty infiltration in the liver. He believes however, that their lipotropic activity is not due to either presence of B_{12} or choline but must be due to other unidentified constituents.

Cornatzer in his review* of the newer work on phospholipid synthesis states that choline containing phospholipids are probably an integral part of enzyme systems necessary for oxidation of fats and fatty acids. The lipotropic effect of lecithins appears to be on the metabolism of fatty acids in the liver rather than by enhancing their mobilization in the form of plasma phospholipids. In animals fed low protein diets there is usually a decrease in level of total phospholipids in the liver. The effect is especially marked in lecithin fraction with consequent lower ratio of the choline containing, to the total phospholipids.

The effect of low protein diet or a normal diet for 9 days seems to influence little the rate of synthesis of plasma phospholipids in men. In plasma there are primarily choline containing phospholipids while in the liver both choline containing and non-choline containing phospholipids are abundant. The synthesis of choline containing fraction in animals on low protein diet is practically the same as on stock diet except when guanidioacetic acid or diethanolamine were added. (methionine is also the methyl donor for synthesis of creatine from guanidioacetic acid) then a marked decrease in synthesis of choline containing fraction occurred. Diethanolamine apparently acts as metabolic antagonist to ethanolamine for formation of lecithins and natural cephalin. The rate of lecithin synthesis by the liver of rats is related to activity of choline oxidase, or to the role of natural inhibitors such as fatty acids. The diminished choline oxidase activity permits an adequate rate of synthesis of choline containing phospholipids. Absence of this enzyme in guinea pigs makes production of fatty liver in this species impossible. The liver is more efficient with the lecithin molecule when liver is fatty even though a decrease in total phospholipid occurs (as measured by labeled P^{32}). The measure of phospholipid synthesis in the liver is a crude test of its function since much stress is required for its alteration. The phospholipid synthesis in plasma of untreated cirrhotics is very similar to that of normal individuals. The synthesis of liver phospholipids in normal persons, maintained on various diets is constant when expressed per gram of fat free tissue. Studies of incorporation of P^{32} into the liver phospholipids and nucleoproteins of rats have revealed that the liver phospholipids P/N was constant irrespective of the protein or fat content in the diet. The ratio of the relative specific activities of the phospholipid P/nucleoprotein P was unaltered by the protein intake or the amount of fat in the liver. Campbell and Kosterlitz have shown that the phospholipid P content of a unit of liver cell is determined mainly by the dietary protein intake, a little by the fat intake and not at all by the choline content of the diet. The phospholipid P/protein N ratio is constant over a wide range of dietary protein intake. There appears to be a constant relation of the synthesis of phospholipid to that of nucleoprotein whether or not the liver is "fatty", fibrotic or normal. While dietary intake

seems to have little influence on this process, thyroid hormone increases the rate of synthesis and thiouracil and thiourea diminish the phospholipid turnover. In cirrhotic patients with fatty infiltration a significant increase in *phospholipid synthesis is demonstrable after a single dose of choline or methionine.

Lipid phosphorylation is greatest in conditions in which a single dose of lipotropic agents is administered in the presence of "fatty liver." The choline effect is chiefly due to an increase in the rate of formation of lecithins. Also certain monlipotropic substances increase the turnover of liver phospholipids (cystine, thanolamine and diethanolmine). This stimulating effect of lipid phosphorylations doesn't occur in rats on stock diet or in man on adequate protein diet.

Apparently the rate of synthesis by the liver cell is rather constant when related to a unit of tissue or nucleoprotein and is not influenced by protein content of the diet fat content of the liver or the degree of fibrosis.

This effect may represent a replacement of a deficiency of methyl donors or methyl acceptors or merely a mass action effect.

Clinical aspects of Kwashiorkor

It is now generally agreed upon that there is a distinct clinical and pathological disease process which is very common in certain tropical countries called kwashiorker. The term kwashiorker was chosen upon recommendation of WHO of the United Nations. FAO/WHO surveyed the parts of Africa South of the Sahara, covering a broad zone of central or Tropical Africa from Zanzibar to Dakar, Kenya, Uganda, Ruanda Urundi, Belgian Congo, French Equatorial Africa, Nigeria, Gold Coast, Liberia, Gambia and French West Africa (Senegal). Brock of the University of Capetown and Autret of the FAO with a large team of investigators conducted this survey. It was stimulated by the highly disturbing frequency of this deficiency syndrome among infants and young children in Africa with high mortality rates. Kwashiorkor as a deficiency disease is by no means a new one nor is it confined to the tropical belt. It has been described in Europe. Recently an epidemic occurred during the siege of Budapest in starving children and was ably described by Veghelyi.

It has also become clear that a syndrome described by Czerny and Keller in 1906 in Germany and called Mehlnahrschaden was identical with the syndrome of kwashiorkor. In South America, India and even in the United States the syndrome has been observed and frequently classified as "nutritional edema".

Dr. Cicely Williams published her experiences among the Ga people of the Gold Coast in 1933. The illness was called kwashiorkor by this tribe, which means "red boy", implying the pigment disturbances associated with this condition. It is however known under a number of different names such as malignant malnutrition, polydeficiency disease, M'buaki, syndrome depigmentation-oedeme, infantile pellagra, Bouffisure d'Annam, musanvu ("the disease of the displaced child") etc. The term infantile pellagra is very mislead-

*The above summary of the work on phospholipid synthetis is freely quoted from an excellent review by W. E. Cornatzer and represents the results of numerous investigations.

ing since kwashiorkor in spite of skin lesions resembling pellagra is entirely distinct from it. The task of the investigating team was to establish the relationship of dietary habits, composition of the diets, diets during pregnancy, lactation, infancy and childhood to the incidence of kwashiorkor. Also to enquire about the cases of nutritional edema, dyspigmentations of skin or hair, liver disease of obscure etiology, hypoalbuminuria, etc. Also the attempt was made to correlate the incidence of adult cirrhosis and primary carcinoma of the liver with the high incidence of kwashiorkor in certain areas.

Following diagnostic criteria were suggested by Brock and Autret: kwashiorkor is a nutritional syndrome or syndromes found among indigenous Africans in which characteristically the following signs occur.

1. Retarded growth in the late breast feeding, weaning and post-weaning ages with
2. alterations in skin and hair pigmentation,
3. edema,
4. fatty infiltration, cellular necrosis or fibrosis of the liver,
5. heavy mortality in absence of proper dietary treatment and
6. frequent association with a variety of dermatoses.

Retardation of growth This manifestation, although frequent and fundamental, is also present in other forms of malnutrition. Trowell maintains that he has never seen a case of kwashiorkor in which growth was not seriously retarded. Yet in spite of that the infant does not look emaciated or starved. Subcutaneous fat is often quite considerable and especially in the presence of early edema a false impression of reasonably good nutrition may be obtained. However in the stage of recovery after the disappearance of edema apparent gross atrophy and failure of muscular development become manifest. It should be noted that while the growth and development of African children progresses equally well to European children up to the age of nine months, there is subsequent retardation of weight and stature which reaches its maximum at the age of five years.

Dyspigmentation This term applies to a) depigmentation-reduction of the brown pigment of Negro skin and b) dyspigmentation-change in the quality of the pigment. Both these features appear in the skin and hair. It may be diffuse or patchy. There is strong evidence supporting their nutritional origin as distinguished from genetic hypopigmentation. It may occur without changes in the texture or with alteration of the texture. The alteration in color may be more clearly seen around the temples and over anterior part of vertex giving golden halo effect. Also seen is the gray to white discoloration of the hair which is regarded as a more severe manifestation of kwashiorkor than the red. Crinkly wool, firm texture of the hair of healthy Africans changes into finer, more silky texture with loss of curves. In some cases dyspigmentation shows itself as a reddish hue. Hair dyspigmentation is the more convincing evidence of malnutrition being the responsible factor. There are at least three nutritional factors affecting color and texture of hair, one affecting the texture and possibly two affecting the color. Proper feeding may restore normal texture and color within six months to a year, as long as it takes the new hair to grow. This sign there-

fore persists beyond the other signs of kwashiorkor which tend to disappear earlier. In conclusion it is believed that these changes are related to protein deficiency.

Edema and hypoalbuminemia Albumin level has been invariably markedly reduced in kwashiorkor with edema. Association of hypoalbuminemia and edema seems to be universal. The recording of total plasma protein is of no value since frequently there is a compensatory rise in serum globulin which may be equal to the drop in albumin. The hypoalbuminemia is regarded in these areas as a result of parasitic infestation especially malaria, however it is seen without parasitosis. There are no effusions into serous cavities. Edema tends to be generalized involving early the face and feet. This edema cannot be explained by cardiac or renal disease. There is only a trace of albumin in the urine.

Liver changes Many authors have stressed the invariably present fatty infiltration of the liver in kwashiorkor. The size of the liver may vary from lack of clinical enlargement to moderate enlargement. In many cases the abdominal distension may obscure hepatomegaly. However when the liver is examined by biopsy or at autopsy marked fatty infiltration is always seen in any severe case of kwashiorkor. Liver biopsy studies in Kampala and Johannesburg showed disappearance of fat as treatment was successfully carried out. Waterlow in his study of a related syndrome in Jamaica recognized this fundamental aspect of the disease and coined the term "fatty liver disease" for this syndrome.

Dermatosis This term includes all skin lesions seen in kwashiorkor. There is disagreement among investigators as to whether the dermatosis is or is not related to pellagra. Brock concludes that the dermatosis represents only an associated condition of multi-etiological nature, which differs in different parts of the continent. According to Trowell's description the commonest form consists of an eruption occuring in sharply defined black varnished patches on the areas exposed to irritation but not in areas exposed to sunlight where classical pellagra would appear. The black islands rapidly enlarge, tend to coalesce and then peel to disclose a white or pink area underneath. Spontaneous peeling appears quite independently of any specific therapy, although this usually occurs when the patient's condition is improving. This "enamel paint dermatosis" or "erosive dermatosis" is peculiar to kwashiorkor. Dermatoses are not present in all cases. They are considered a result of a complex deficiency rather than of one element in the diet.

Gastro-intestinal manifestations A variety of vague gastro-intestinal symptoms was recorded. The appetite in advanced cases is always very poor. The abdomen is usually distended. Diarrhea is variable, usually mild or absent but in some areas severe, depending on the food eaten and the presence of a superimposed infection. Undigested food is passed in bulky or loose stools which may be frequent. Mild degree of steatorrhea is encountered but on diets free of fat it has not been reported. Diarrhea and nutritional deficiency form a vicious cycle. There is reduction in all pancreatic enzymes, in plasma esterase, plasma lipase, in serum amylase, cholinesterase and alkaline phosphatase. Blood urea, total cholesterol and cholesterol esters are reduced.

Mental dullness Trowell says, describing the mental state of a child with kwashiorkor "The mother unwraps a miserable imp who immediately grizzles and cries and avoids the light" . . . "mental apathy until disturbed, then often irritability". Clark commented that "the mental changes found in kwashiorkor are the most constant and probably one of the most important of all the changes seen" . . . "They are, I think, far more constant, characteristic and important than the skin changes about which so much has been written" . . . "If one can get a smile out of a child with kwashiorkor, one can assume it is well on the way to being cured" . . . "Peevish mental apathy" aptly describes the mental state of the patient.

Anemia Slight, normocytic or slightly macrocytic anemia is encountered in absence of associated parasitic infections. In association with ankylostomiasis severe chronic blood loss anemia is present. Also hematuria from bilharziosis in Nigeria is considered even more contributory to hypochromic anemia than ankylostomiasis. Trowell described dimorphic anemia which is characteristic of kwashiorkor in Kampala. Lehman has attributed the dimorphism to the presence of reticulocytes. This explanation was not found satisfactory. Price Jones curves show strikingly biphasic shape and Charles maintained that it is not due to presence of reticulocytes.

Incidences The milder forms of kwashiorkor are, according to Trowell, so common that many doctors would regard the manifestation of retarded growth in the second year of life, brown soft hair, pale skin and low serum albumin as normal. If this is a true appraisal of the situation then in certain parts of Africa it is probable that the majority of children in the second and third year of their lives suffer from kwashiorkor. But even if this term is reserved to the severest forms of the disease it is still an important syndrome and one can only guess that the number of severe classical cases of kwashiorkor must be considerable in number. It is of interest to note that the disease is present in nearly 5% of children in Southern Italy (Frontali).

Mortality Heavy mortality has been recorded in severe cases of kwashiorkor especially those with edema and fatty liver. It is generally assumed that heavy mortality is due to irreversible liver disease. In two centers, Johannesburg and Pretoria, mortality ranged from 30-40% until recently. In other parts of Africa mortality ranged from not less than 30% to as high as 100% as reported by Pieraerts in Belgian Congo in absence of therapy. Since the introduction of skim milk therapy in the form of lactic acid skim milk powder, in South Africa mortality has fallen rapidly. Figures reported recently by Walt and Ass. in Durban are 2.8% exclusive of cases dying in the first 24 hours.

Pathology in Kwashiorkor The liver in a newborn African child does not differ from that of European infants except for the deposition of malaria pigment which delineates the periphery of lobule. The early changes appear in the weaning period. At this time concomitantly with the clinical signs of deficiency fat droplets begin to appear in the periphery of the lobules, leaving the row of cells at the lamina limitans around the portal triad intact for a considerable period of time. As the deficiency progresses the fat droplets increase in size involving the cells lining the sinusoids progressing grad-

ually towards the central vein. In very severe cases the entire lobule may be infiltrated by fat forming small fatty "microcysts". Lymphocytes wander into the sinusoids in large amounts during the active process. Their role in fat transport is obscure. It may be related to their content of lipases. Davies believes that there is a connection between rapid fat removal from the liver and presence of lymphocytes. Also plasma cells, macrophages, neutrophiles and eosinophile polymorphnuclear cells are seen. The latter two are present especially if an infection complicates the picture. This fatty and cellular infiltration of portal triad seems to be most characteristic and most persistent change which is also seen in livers of clinically not ill African adults. Also portal triads show presence of nuclei of fibroblasts.

Reticulin framework in periphery of the lobules undergoes following changes: Thickening, splitting and reduplication of the fibres. Depending upon the stage of the disease these changes may be either confined to portal triad alone or may involve the entire periphery of the lobule. The peripheral cells as well as the cells of the membrana limitans undergo strangulation by the thickened reticulin and disappear with the collapse of the reticulin structure. Collagenous change appears in the reticulin substance, marking the outline of the lobule. This change however, never reaches the stage of severity in children that it would fall into the category of cirrhosis. The livers of most Africans above the age of two show evidences of fibrotic scarring in portal areas. Portal triads are join together by fibrous strands around the boundary of the lobule. So called stellate fibrosis develops which is the hallmark of kwashiorkor, as Davies calls it. Davies believes that intensely fatty livers are present in young children with little fibrosis and cellular infiltration while more fibrosis and cellular accumulation is more prominent in older children and adults. Some believe that there is iever necrosis in kwashiorkor liver. Fatty liver in children can apparently give rise to monolobular cirrhosis. In such a case the liver consistency is very hard, stony grey color with finely granulated surface. Parasitic involvement as well as Infections such as tuberculosis complicate the picture to such an extent that African liver has been called "histological nightmare." Other important changes occur in the pancreas which shows extreme degree of atrophy long preceding fatty metamorphosis, continuing long after disappearance of fat from the liver. The pancreas is grossly atrophied with marked atrophy of the enzyme secreting cells, zymogenic granules and the cystoplasm of cells. In severe cases pancreatic cells contain no secretory substance whatsoever. Subsequently pancreas undergoes sclerotic changes by proliferation of fibrous tissue. There is no morphologic resemblance to cystic fibrosis of the pancreas. The same atrophy is seen in the parotid gland. In the kidneys there is frequently hyalinization of glomeruli. Adrenals show changes consisting of increase in size of cortex with absence of pigment in juxta-medullary zone. The cardiac muscle shows most interesting changes of degeneration of hydropic type, necrosis and fibrosis. There is no cardiac hypertrophy in contradistinction to endocardial sclerosis with hypertrophy seen in the U.S. The pathology of the gastro-intestinal tract has not been clearly described because of diffi-

culty in interpretation of the post mortem findings. The atrophy of the intestinal mucosa has been described but can not be accepted without confirmation. Cheilosis, angular stomatitis and general stomatitis suggestive of pellagra or ariboflavinosis have been described. It is worth mentioning that in spite of tremendous incidence of cirrhosis in Africa no portal hypertension has been observed. Davies maintains that in the last 20 years there was not a single death in his vast experience, due to ruptured varices. This is not true for a syndrome related to kwashiorkor that was described by Gyorgy in Jamaica.

Etiology, Pathogenesis, Therapy and Prevention Kwashiorkor is a distinct member of a big group of diseases referred to as diseases of protein malnutrition. It occurs mainly in young children after a prolonged consumption of diets lacking variety, and in which the proportion of protein, especially that of animal origin, has been low and the proportion of carbohydrates may have been high. These diets always have a low protein-calorie ratio and a very low animal protein-calorie ratio.

While children are protected from the disease during the period of breast-feeding the disease occurs shortly after cessation of breast-feeding. Early second pregnacy means death to the first child. It is customary in many parts of Africa to put children immediately after cessation of breast-feeding on adult diets. In areas in which cassava, plantains, bananas and sweet potatoes constitute staple foods, kwashiorkor and protein deficiency is likely to occur. When food stuffs contain less than 2 gms. of protein/100 calories, protein deficiency is almost inevitable unless staple is supplemented by reasonable quantities of protein rich foods. Because of the fact that aminoacid content and composition varies from food to food there is no quantitative ratio between amount of protein in the diet and kwashiorkor. The factor of digestibility plays an important part. Age and protein requirement consideration is important because growth in infancy, childhood and adolescence increases protein requirements as compared to adults. Kwashiorkor is prevalent in the first five years of life. It may be related to the fact that cow-milk which is the best source of protein in the post-weaning period, is lacking in Africa. Although the evidence seems to be suggestive that absence of certain essential aminoacids, especially methionine, may be responsible for this deficiency syndrome, studies of the African diets strongly indicate that multiple deficiencies are present. The remarkable curative effect of milk protein narrows down the number of factors which should be considered. The missing factor or factors are contained presumably in skim-dry milk. Its additional value in severe cases is based upon the fact that no pancreatic enzymes are required for its digestion. Vitamin A deficiency appears to be very common in cases of kwashiorkor in Asia. Riboflavin deficiency appears on maize diets. In general vitamin deficiencies are seldom seen except in terminal states of kwashiorkor, and it should be noted that signs of vitamin deficiency seldom occur in cases dying of general undernutrition due to caloric deficiency. Hence administration of vitamins without protein is useless in this disease. It is also doubtful whether any specific response has been demonstrated to methionine, choline, vita-

min B_{12}, or folic acid. All the features of the disease, and particularly those involving the organs which have the highest protein turnover respond to protein rich diets, especially milk protein and other animal protein. Treatment of associated infections and parasitic infestations is of outstanding importance. Davies believes that the basic lesion in kwashiorkor seems to be the selective atrophy of the enzyme secreting glands affecting the pancreas, the small intestines, salivary and lacrimal glands. The cause of this atrophy is unknown. Also unknown is the relationship of the fatty infiltration to the preceding enzyme cell atrophy, and to the factors that enhance the removal of fat in the liver. The crucial human experiment is still forthcoming. In conclusion one can use the statement quoted by Gillman & Gilbert which aptly illustrates the problems involved in human malnutrition: "No sign from heaven is likely to point out one key that unlocks the elementary activities. The theory that a single governor exists for a physiological activity does not appear now to be substantiated. Moreover, there is no means of recognizing a regulator even if examined. A specific volley of nerve impulses or an isolatable extract are possible links in the chain or elements in a complex. Repeatedly it is found that many factors vary simultaneously; each one is as central as any other, only by convenience of thought is one exalted above another." (Observations of Adolph made in connection with water metabolism.)

Bibliography

W. S. Hoffman "The Biochemistry of Clinical Medicine" 1954

H. A. Harper "Review of Physiological Chemistry" 1951

H. P. Himsworth "The Liver and its Diseases" 1950

Klaus Schwartz "Introduction: Liver Necrosis Versus Fatty Liver and Cirrhosis" Ann. of the New York Academy of Sciences Vol. 57, Art. 6 P:617

F. S. Daft "Experimental Differentiation between Liver Necrosis and Liver Cirrhosis and Some Dietary Factors Affecting Their Development" Ibid P:623

W. S. Hartroft "The Sequence of Pathologic Events in the Development of Experimental Fatty Liver and Cirrhosis" Ibid P:633

C. H. Best, C. C. Lucas, and J. H. Ridout "The Lipotropic Factors" Ibid P:646

V. A. Drill "Lipotropic Effects of Vitamin B_{12} and other Factors" Ibid. 654

J. N. P. Davies "The Pathology of Dietary Liver Diseases in Tropical Africa" Ibid: P:714

H. C. Trowell "Clinical Aspects of the Treatment of Kwashiorkor" Ibid. P:722

H. C. Trowell, T. Moore, and I. M. Sharman "Vitamin E and Carotenoids in the Blood Plasma in Kwashiorkor" Ibid. P:734

J. Gillman and Ch. Gilbert "Aspects of Nutritional Liver Disease—Human and Experimental" Ibid: P:737

J. C. Waterlow and S. J. Patrick "Enzyme Activity in Fatty Livers in Human Infants" Ibid. P:750

B. M. Nicol "The Question of Relative Importance of Protein and Labile Methyl in the Development of Fatty Liver and Cirrhosis in Man" Ibid. P:764

W. E. Cornatzer "Phospholipid Synthesis in Liver Metabolism" Ibid. P:919

J. F. Brock & M. Autret "Kwashiorkor in Africa" WHO Monograph Series 1952

H. Elias "A Re-Examination of the Structure of the Mammalian Liver" Am. J. Anat. 85:379 1949

W. S. Hartroft "The Escape of Lipid from Fatty Cysts in Experimental Dietary Cirrhosis" Transaction of the Ninth Conference, "Liver Injury" Josiah Macy, Jr. Foundation, 1950

J. N. P. Davies "Kwashiorkor" Ibid. P:151

P. Gyorgy "Vitamin B_6, Folic Acid and the Lipotropic Agents" Ibid. P:206

H. Popper "Discussion: Development of Tra-

Beculan in Cirrhosis and Pancreatitis due to Protein Deficiency" A Ciba Foundation Symposium "Liver Disease" 1951

W. A. E. Karunaratne "Discussion: Aetiology of Cirrhosis in Ceylon" Ibid. P.106

L. E. Glynn "Experimental Hepatic Cirrhosis" Ibid. P.74

A. Czerny & A. Keller "Des Kindes Ernahrung, Ernahrungsstorungen u. Ernahrungstherapie" (1906), 2nd Ed. 1928

E. T. McEnery "J. Pediat. 2: 478" 1933

P. V. Veghelyi "Ann. Pediat. 175: 349" 1950

C. D. Williams "Arch. Disease Childhood. 8: 423" 1933

Other investigators mentioned in this review were quoted in the above references.

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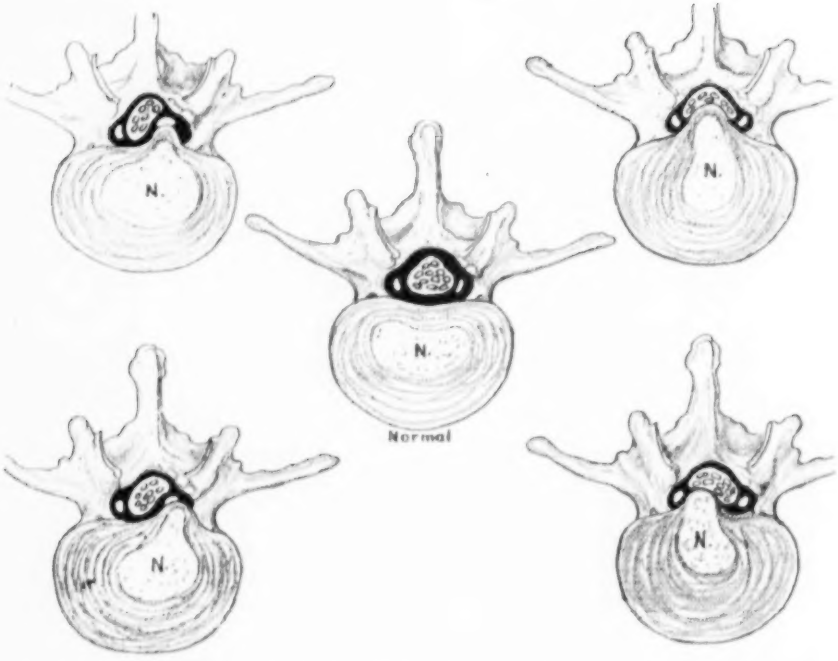

Pathological variations of the ruptured intervertebral disc as compared with normal position.

Primary Carcinoma of the Pancreas

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In recent years there has been an increasing awareness of the clinical picture produced by carcinoma of the pancreas, largely as a result of its clarification in the literature. Thus, diagnoses are being made at an earlier stage in the course of the disease with greater hope for surgical removal.

Incidence and Distribution

[1, 2, 3, 4, 5, 6] In general it may be stated that primary carcinoma of the pancreas causes from 1 to 2 per cent of all deaths in the population at large, is present in about 0.1 per cent of all patients admitted to large general hospitals, is noted at from 0.3 to 0.75 per cent of all autopsies, and comprises from 1 to 2 per cent of all carcinoma.[1] Hick and Mortimer[2] and Arkin and Weisberg,[3] however, suggest that carcinoma of the pancreas forms about 5 per cent of all cases of malignant disease. The incidence of carcinoma of the pancreas in regard to all carcinomas of the abdomen is 6 per cent (Malinowski).[4]

Strang and Walton[5] reporting on the Newcastle series noted that 0.32 per thousand hospital admissions were diagnosed as carcinoma of the pancreas, 0.65 being carcinoma of the head and 0.17 carcinoma of the body or tail. They also found an incidence of 0.5 per 1,000 autopsies for all pancreatic carcinomas, including 2.3 per 1,000 for body and tail. Hick and Mortimer[2] observed 6.3 per thousand for all primary pancreatic neoplasms at Cook County Hospital in Chicago. Duff,[6] in the Johns Hopkins group, encountered only 3.6 per thousand autopsies including 1.36 per thousand for body and tail.

Duff futher attempted to compare the incidence of growths in the body and tail with that in the head by listing the cases described in 14 reported series. He pointed out that great variation between individual series could be accounted for by the fact that in some cases the diagnosis was clinical, in others it was made at autopsy. The clinical series included a preponderance of neoplasms in the head, since the latter are more easily diagnosed than those located in the body or tail, while pathological series revealed an undue proportion of growths in the body and tail. Duff concluded that approximately 3 times as many malignancies occurred in the head as elsewhere.

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Age, Sex, and Race [7, 8, 9, 10, 4, 5, 11, 12, 13.] The greatest number of cases of pancreatic carcinoma occur in persons in the sixth decade and the average age is approximately fifty-six years. The youngest case of carcinoma of the pancreas described in the literature was that of a seven month old female reported by Mielcareck.[7]

Men are more frequently affected than women with a ratio of about 2.5:1. Miller,[8] Burke and Plummer,[9] and Brown *et al.*[10] in independent studies reported an incidence of 2.6:1, Malinowski[4] 2:1, Duff[5] 3:1. In a large series Thompson and Rodgers,[11] however, noted an incidence of only 1.5:1 and surprisingly, Moore and Younghusband[12] noted a slight preponderance of females over males.

It was formerly believed that the disease was rare among the Negro race but recent reports contain a high percentage of Negroes and in some there is a predominance of Negro patients in relation to the proportion of general hospital admissions. (D. H. Clark[13]).

Etiology [14, 15, 16, 17, 1, 4, 18, 19] The origin of carcinoma of the pancreas has not been definitely determined but there are several predisposing factors that have been suggested and evaluated, factors which may be of importance in the initiation of the neoplasm.

1. Developmental errors—Grauer[14] postulated that developmental errors may occasionally be responsible because of the complex origin of the pancreas.

2. Grauer further proposed that, during the process of recurrent waves of loss and hyperplasia of tissue which the pancreas continually undergoes, some portion of this organ may suddenly lapse into uncontrolled reproduction.

3. Aberrant pancreatic tissue—the proposal was made by Ewing[15] that aberrant pancreatic tissue often found in the duodenal mucosa and around the head of the pancreas may be the initial site of certain neoplasms, especially those involving both the duodenal wall and the pancreas.

4. Chronic pancreatitis is often found in glands which are the seat of malignancy. During the process of repair following chronic inflammation it may be possible for a group of hyperplastic cells to pass beyond its normal limits and proceed to multiply rapidly. Doubilet *et al.*[18] reported several known cases of chronic pancreatitis who subsequently developed carcinoma of the pancreas. In some of their series, however, chronic pancreatitis was a coincident finding at autopsy, raising the question, as has been frequently done by others, of whether the chronic pancreatitis precedes or is secondary to the development of the neoplasm.

In those cases of carcinoma of the head of the pancreas where obstruction of the bile and pancreatic ducts is a prominent feature, there eventually results an accumulation of mucous secretion and pressure on the essential epithelium of the glands. The acinar tissue is destroyed in two or three weeks. Unlike pancreatitis, in which there is no permanent obstruction and in which marked regeneration follows necrosis of the acinar cells, carcinoma of the head with its persistent and usually complete obstruction leads to atrophy and fibrosis of acinar tissue without any evidence of regeneration.

Knight and Muether[17] in their study of cases of carcinoma of the pancreas versus cases of chronic pancreatitis noted that the latter disease affects

males and females equally, while in carcinoma the incidence of males is higher, suggesting to them that chronic pancreatitis does not predispose to carcinoma.

5. Chronic cholecystitis—According to Berk,[1] approximately 10 to 15% of all patients with primary carcinoma of the pancreas demonstrate evidence of chronic cholecystic disease. Malinowski[4] reported that in his group of carcinomas of the head of the pancreas 43% had previous biliary tract disease. However, biliary tract pathology is present in 20 to 25% of the adult population and the incidence increases with age (Ulin *et al.*[18]). Doubliet *et al.*[16] noted that several of their patients with carcinoma of the pancreas had previous cholecystitis. At any rate, the import of the association of chronic cholecystitis with carcinoma of the pancreas depends solely on the frequency with which pancreatis accompanies disease of the gallbladder.

6. Alcoholism—Malinowski[4] stated that 20% of his cases of carcinoma of the head of the pancreas were alcoholics. Alcohol stimulates the pancreas to secrete highly concentrated pancreatic juice. Excessive use of alcohol is frequently noted in patients with chronic fibrotic changes of the pancreas.

7. Diabetes mellitus—It has been suggested that diabetes mellitus may be a predisposing factor. A history of long-standing diabetes is found in 7% of patients with carcinoma of the pancreas, according to Berk.[1] There are some who believe that the association is coincidental. Marble[19] stated that the pancreas is the most common site of a malignant condition in diabetics. In these patients the pancreas is the seat of a carcinoma 6 to 16 times as often as in the population at large.

8. Food, food products, and dietary habits—The questionable role of these still remains unanswered and bears further investigation.

Pathology [1, 9, 8, 11, 5, 20, 21, 22, 23, 24, 25, 26, 27, 28.] Carcinomas of the pancreas are extremely variable in appearance and size. Some bulge from the surface; others produce firm, retracted, scarified areas. Some are large and sharply demarcated while others have so invaded adjacent structures that the pancreas is matted in a mass of tumor tissue. The head is the most frequently involved portion of the gland, as noted above. Berk[1] lists the incidence as 70 to 75% and most authors concur. Burke and Plummer,[9] however, found that the majority of their cases involved the head, body, and tail and it was difficult to determine the primary site. Indeed, there is frequently much overlapping of regions of involvement and many observers prefer not to differentiate among the various portions of the gland.

Usually the lesion is scirrhous, almost gritty to the knife edge, and fibrous in appearance (Duff[8]). The histologic type in these cases is generally the cylindric-cell adenocarcinoma which arises from the epithelium of the pancreatic duct system. This type of tumor is composed of irregular duct-like spaces lined by cuboidal or columnar epithelial cells. Occasionally the neoplasm is medullary in nature with a soft consistency and fleshy cut surface, showing, at times, irregular areas of necrosis and hemorrhage. In rare instances the tumor has a gelatinous mucoid character. Microscopically these usually appear as acinar-cell adenocarcinoma, consisting of masses of polyhedral or rounded

cells which may form regular rows or small clusters suggestive of pancreatic acini. Rarely, metaplasia is shown with the formation of squamous epithelial cells. The islets escape involvement. They are usually hypertrophied and may be seen in greater numbers than usual.

Modes of Spread—In general, carcinoma involving predominantly the body and tail tends to extend more massively and metastasize more widely than does that in the head. Duff[5] discussed the subject of metastases in great detail, pointing out that spread occurred via perineural spaces, lymphatics, veins, and by direct extension.

(a) Direct extension—Carcinomas of the pancreas tend to adhere to and infiltrate adjacent structures. The duodenum, stomach, and colon are commonly pressed on and invaded, sometimes with penetration to the lumen and production of ulceration. As would be expected, duodenal infiltration is more common in carcinoma of the head of the gland. Peritoneal implantation resulting in ascites is frequent, especially if the body or tail is involved, as reported by Thompson and Rodgers.[11] Strang and Walton,[21] however, had a low incidence of ascites in their group of cases of carcinoma of the body and tail.

(b) By way of the lymphatics—Lesions in the head spread to the subpyloric nodes. Those in the body and tail metastasize mainly to the gastric, hepatic, coeliac, mesenteric, periaortic, and even the mediastinal and peribronchial nodes. Supraclavicular nodes are sometimes affected but not as commonly as in carcinoma of the stomach.

(c) By way of the blood vessels—The most frequent vascular spread is to the liver via the portal vein. Embarrassment of the portal circulation may occur if there is marked obstruction of the intrahepatic radicles of the portal vein by neoplastic thrombi. The venous drainage may carry tumor cells from the liver to the lungs then via the arterial system to the adrenals (fairly common), kidneys, spleen, bones, etc.

(d) Along nerve sheaths—As a means of distant spread this method does not assume much importance. However, its significance lies in the production of the abdominal pain which is so prominent a clinical feature. The posterior surface of the body of the pancreas is in direct relation to the coeliac plexus and is immediately adjacent to the nerves entering and emerging from this plexus. More will be said about this below.

Venous thrombi—In recent years there has been a recognition of the frequent association of venous thrombi with carcinoma of the pancreas, especially of the body and tail. Sproul[20] first emphasized this relationship. In her report of cases of carcinoma of the body or tail 56.2% showed thrombosis of some vessel and 31.3% showed many thrombosed vessels in various parts of the body. Her group of cases of carcinoma of the head contained only 9.7% with multiple thromboses.

Similar findings were reported by Kenny[21] who noted multiple venous thrombi in 33% of cases of the body or tail and no multiple thrombi in patients with growths in the head. Thompson and Rodgers[11] stated that multiple thrombi may be found when the tumor arises in the head but with less than half the frequency when it is primary in the body or tail.

Wright,[22] apparently, is at variance

with the expressions of others. He stated that in his experience position of the neoplasm in the pancreas is of no importance in the occurrence of intravascular coagulation.

Sproul noted that the explanation for the thrombi on the basis of the presence of tumor cells in the vessel walls, on inflammation of the vessel walls, or on mechanical obstruction of the vessels from the growth of the primary neoplasm, was rarely justified. There was no correlation between age, sex, or race and the formation of thrombi.

Several suggestions have been advanced for the situation and for the frequency of thrombi in carcinoma of the body or tail. Sproul,[20] Leach[22] and Miller *et al.*[24] did not note any histologic difference between the types of carcinoma occurring in the head and elsewhere in the pancreas. Jennings and Russell[23] and Kenney[21] postulated that the clotting tendency is the result of the formation of coagulative factors by the neoplasm and their release into the circulation. They believed that mucus-producing columnar cell carcinomas were the source of these substances. However, it has been demonstrated by Duff[5] and others that mucin formation occurs in the growths of ductal origin which comprise the majority of tumors of the head as well as of the body and tail of the pancreas.

Miller *et al.*[24] sought to explain the differing incidence of thrombosis in head and body or tail lesions on the frequent occurrence of jaundice with lesions of the head and the more prolonged course of malignancy of the body or tail. This suggestion, however, fails to account for the more striking disproportion of thromboses when carcinomas of the body or tail are compared with other visceral malignancies in which neither jaundice nor comparative length of survival are factors.

Gore[25] stated that, as a rule, carcinoma of the head produces ductal obstruction and secondary atrophy of practically all acinar elements; however, when the neoplasm is in the distal portion of the gland, the proximal portions of the gland retain their morphologic structure. Significantly, Sproul[20] found an anomalous duct permitting normal acinar tissue to persist in 2 of her 3 cases of carcinoma of the head associated with thrombosis. The position of pancreatic malignancy is of import, therefore, only to the extent that survival of sufficient intact glandular tissue is permitted. In a study from Salt Lake County General Hospital it was noted that 50 per cent of their cases with secondary carcinoma of the pancreas also had thrombosis; thus as long as carcinoma of various origins fulfils the criterion of infiltrating functional pancreatic tissue, it is as often associated with thrombosis as is primary pancreatic carcinoma.

Generally, the pancreatic neoplasm is surrounded by a zone of reactive pancreatitis. Accompanying pancreatitis, there is a rise of serum amylase and lipase. Destruction of the gland by massive neoplastic invasion or by obstruction of the ducts nullifies the elevation. Gore's theory, which is among the most tenable of those suggested, is that, besides the elevation of serum amylase and lipase produced because of the reactive pancreatitis, there is also a rise of trypsin. Little attention has been paid to trypsin levels as amylase and lipase determinations are simpler and because blood normally contains a large quantity of antitryptic substances.

When trypsin is rapidly injected intravenously, it acts like thromboplastin and causes massive intravascular clotting and death. There is, of course, no anologue in naturally occurring disease processes. Trypsin is never released in such marked quantities. Generally, the slower release of trypsin provides the body with time to increase its output of antitryptic substances, the latter being normally present in the serum. Therefore, in acute pancreatitis, there is protection from the clotting effects of trypsin. Innerfield *et al.*[27] suggested that rise in level of blood antitrypsin occurring in pancreatis be measured and used as a diagnostic procedure.

In carcinoma of the pancreas there is a slow but constant release of trypsin into the circulation. As noted before, there is a compensatory increase of antitrypsin, but, to complete Gore's theory,[26] over a prolonged period where progressive debilitation is the rule, there may be a failure of this mechanism. The nutritional disorder which so frequently accompanies carcinoma may have a deleterious effect on liver structure and its function. He suggested, then, that the clotting tendency is the result of the failure of the antitrypsin mechanism.

Recently McKay *et al.*[28] reported a case of a 56-year-old female with carcinoma of the body of the pancreas who died of severe hemorrhage due to fibrinogenopenia. At autopsy numerous fibrin deposits were found in the hepatic sinusoids, in the spleen, and in the arterioles of the rectal mucosa. There were also vegetations on three of the heart valves and a portal vein thrombosis. The fibrinogenopenia may be explained by the widespread fibrin deposition. From this and other reports it would appear that carcinoma patients are prone to hemorrhage caused by fibrinolysins or fibrinogenopenia, the latter following fibrin deposition or destruction of fibrinogen by a circulating fibrinolytic enzyme derived from the blood or from the tumor tissue.

Symptoms [5, 17, 1, 6, 29, 30, 31, 15, 10, 32, 33, 34, 8, 4, 35, 36, 37, 1]

Duration of Symptoms The average duration of symptoms prior to admission has been reported as from 3 to 6 months. The average duration of illness from the first symptom to death is 7 to 10 months. Of course there is a wide range of duration, some cases being symptomatic for 2 to 3 years prior to admission. The question arises in the latter cases, however, of whether these were not patients with chronic pancreatitis who later developed carcinoma of the pancreas. The average duration of symptoms is similar whether the lesion is located primarily in the head or in the body or tail.

In the following discussion of symptomatology little differentiation will be made between the symptoms in carcinoma of the head and those in carcinoma of the body or tail because they are essentially similar except that jaundice is more common in carcinoma of the head and is likewise more common as an initial symptom.

Initial Symptom Abdominal pain is the outstanding initial complaint. It is found in at least 50 per cent of the patients. In Strang and Walton's series[5] it was the first symptom in 50 per cent. Knight and Muether[17] noted an incidence of 62 per cent. Duff[6] reported an incidence of 87.5%. According to Berk[1] jaundice is the second most frequent initial symptom, being noted

in about 20 per cent of the cases. Knight and Muether[17] found that only 6 per cent of their patients had jaundice as an initial symptom. Berk[29] stated that in 86 per cent of the instances in which both jaundice and pain are present, the pain will have made its appearance before the jaundice. In these cases approximately the same percentage applied even in those in which the head was believed to be the dominant site.

Strang and Walton[5] reported a 15.5 per cent incidence of pain in the back and side as the initial symptom. Other initial complaints which are more infrequent are weight loss, anorexia, diarrhea, constipation, alternating diarrhea and constipation, flatulence, peptic ulcer syndrome [Berk[29] found an incidence of 12 per cent of his cases presenting with a classic ulcer rhythm of pain with relief by eating], dysphagia, vomiting, abdominal swelling, intestinal obstruction, acute cholecystitis [Rothenberg and Aronson[30] found that 9 per cent of their cases in which the common duct was obstructed due to neoplasm presented as acute cholecystitis], psychic disturbances, "lumps" in the skin, peripheral venous thrombosis, and gastrointestinal hemorrhage. Nanson[31] reported an unusual case of carcinoma of the head of the pancreas in a 17-year-old female that presented as gastrointestinal bleeding from an ulcer of the second portion of the duodenum. She had been asymptomatic prior to the hemorrhage.

Analysis of Symptoms

1. **Abdominal Pain** Strang and Walton[5] found it to be present in 71 per cent at some time,[5] Clark[13] in 72%, Brown *et al.*[10] in 73 per cent, Knight and Muether[17] in 74 per cent, Duff[8] in 87 per cent.

Of those that have pain, the majority describe it as being situated in the upper abdomen. It is usually central but may be in the right upper quadrant or the left upper quadrant. It frequently radiates to the back. Back radiation has been recorded in the literature as occurring in from 18 to 50 per cent of patients. The pain, however, may be situated in any part of the abdomen or may be generalized.

Strang and Walton[5] have described the pain as most commonly intermittent, others have stated that it is usually constant. The pain is dull, aching, gnawing, griping, nagging, occasionally colicky or stabbing. Often when an attack subsides, a feeling of soreness remains. The pain is sometimes made better by the ingestion of food, often made worse. It is frequently most severe at night due, as noted before, to the stretching of infiltrated nerves in the horizontal position. For this reason many have found that they often obtain relief by bending forward. Smith and Albright[32] observed that the pain was relieved by sitting up and aggravated by lying down in 43% of their cases but Strang and Walton[5] could not corroborate this. There are occasional reports of the pain being intensified by cold, exertion, defecation, or deep breathing. Some reported relief by eructation, by applying heat to the abdomen, defecating, or vomiting.

As can be noted from the above there is no constancy to the location and character of the pain but, to summarize, it is most generally epigastric, radiating to the back, dull, constant, of moderate severity, and relieved by sitting up and bending forward.

The pain is not only due to nerve infiltration but also to obstruction of the

ducts by the neoplasm. This latter has been studied by Doubilet and others whereby the ducts were obstructed experimentally and pain similar to that described by certain patients with carcinoma of the pancreas was produced.

Duff[6] found that in all of his cases of carcinoma of the tail of the pancreas the pain radiated to the left. In a study by Bliss *et al.*[12] who placed electrodes in the head, body, and tail of 15 of their patients with biliary disease who required surgery and several days postoperatively stimulatetd these electrodes, it was noted that pain from threshold stimulation of the head of the pancreas was located in the upper half of the abdomen and predominantly just to the right of the midline; pain from the body of the pancreas was likewise in the upper half and localized along the midline; pain from the tail was described in both the upper and lower half of the abdomen on the left side. Simultaneous stimulation of all three parts of the pancreas produced band-like pain and pain radiating through to the back. They also determined that right splanchnic block will control pain arising in the head of the pancreas, left splanchnic block pain arising in the tail, and bilateral splanchnic block pain coming from the body of the pancreas. This information is useful in that sympathectomy can be employed to obtain relief from severe pain.

2. Back Pain Only 13.6% of Knight's and Muether's patients[17] had back pains. Strang and Walton[5] reported an incidence of 51 per cent. Most of these also had abdominal pain but in the majority back pain was predominant. Sometimes the pain went through to the back, sometimes it traveled around. Factors which increased or decreased abdominal pain affected back pain in a similar manner. Pain was often described as between the shoulders, less commonly as mid-lumbar, right or left scapular.

3. Substernal and Pleuritic Type Pains have been reported. These are quite uncommon.

4. Jaundice Berk[20] stated that jaundice will appear at some time during the course of observation in about 68 per cent of patients with pancreatic carcinoma. As noted above, icterus occurs less often when the carcinoma involves mainly the body and tail than it does when the head is the principal site. In about one-fifth of all cases of carcinoma of the head, jaundice is not seen at any time. Also in about one-half the patients in which icterus never develops the head of the gland is involved. As everyone knows now, painless jaundice is more uncommon than previously believed. It is found in less than 25 per cent of patients on admission and persists in only about 15 per cent. Miller[8] and Ross[24] emphasized the preicteric stage of the disease. Progressive weakness, weight loss, and pain may precede jaundice by several months.

Clark[13] found that 90 per cent of his cases of carcinoma of the pancreas showed jaundice at some time. Malinowski[4] reported 93 per cent, Knight and Muether[17] 59 per cent, Duff[6] 50 per cent, Smith and Albright [22] 22 per cent, Strang and Walton[5] 19 per cent.

The most common cause of icterus is the obstruction by neoplastic nodes in the porta hepatis or surrounding the common bile duct. Other causes are obstruction of the common bile duct by tumor infiltration, extensive metastases to the liver, etc.

5. Digestive Symptoms

(a) *Anorexia*— has been reported in between 45 and 65 per cent of cases.

(b) *Nausea and vomiting*—have been noted in 12 to 42 per cent. Vomiting is rarely severe and usually of recent development. It does not appear to be a prominent feature.

(c) *Constipation*—This has been stressed to be of frequent occurrence by Duff,[6] Smith and Albright,[32] Ransom,[25] and Strang and Walton.[5] Its incidence is about 39 to 47 per cent. The mechanism of its production is obscure.

(d) *Diarrhea*—is less common and is noted in 7 to 19 per cent. It is more likely to occur in cases of neoplasm in the head due to excess fat in the stools.

(e) *Flatulence*—10 to 15 per cent.

(f) *Abdominal distention*—12 per cent. This is generally due to ascites. Duff[6] and Smith and Albright[32] have commented on the frequency of this association.

(g) *Miscellaneous*—Post-prandial dyspepsia, "heartburn," dysphagia (due to infiltration around the esophagus), abdominal tenderness, borborygmi.

6. Weight Loss Weight loss is the most frequent symptom found in patients with carcinoma of the pancreas. Duff[6] noted it in 100 per cent of his cases, Smith and Albright[32] in 97 per cent, Brown *et al.*[19] in 94 per cent, Strang and Walton[5] in 88 per cent, Knight and Muether[17] in 72 per cent. The weight loss is usually rapid and marked, averaging about 26 pounds.

7. Fatigue and Weakness have been reported in 22 to 58 per cent of cases. Most of these have lost a considerable amount of weight.

8. Psychiatric Manifestations Some patients complain of severe insomnia, depression, fear, and excessive anxiety. Yaskin[36] reported 4 cases in whom these symptoms were noted early in the course of the disease and Ulett and Parsons[27] reported that 10 per cent of their cases had important psychiatric manifestations. They pointed out the superficial resemblance of these symptoms to hysteria. Some cases have been diagnosed as functional disorders due to the bizarre nature of the early symptoms and absence of physical signs and x-ray evidence.

9. Gastrointestinal Hemorrhage Hematemesis and/or frank blood in the stools were noted by Strang and Walton[5] in 17 per cent of their cases. Duff[6] found it in 50 per cent of his cases of carcinoma of the body or tail but in only 12.5 per cent of carcinoma of the head. Knight and Muether[17] found it in 9 per cent of their cases of carcinoma of the pancreas regardless of location. Smith and Albright[32] observed it in only 3 per cent, Thompson and Rodgers[31] in 2 per cent.

It is usually due to infiltration of the gastrointestinal tract either by the primary neoplasm or secondary deposits but it may be due to hypoprothrombinemia or fibrinogenopenia, as mentioned before.

10. Swelling of The Legs due to venous thrombosis has been discussed before.

11. Other Symptoms These are fairly uncommon.

(a) Profuse sweating.
(b) Exertional dyspnea—due to severe anemia.
(c) Pallor—due to severe anemia.
(d) Subcutaneous metastases.
(e) Fever.
(f) Chills.

Physical Findings [5, 1, 17, 6, 4, 28, 29, 22, 19, 29]

1. Icterus

This has been discussed under symptoms above.

2. Emaciation was noted in 71 per cent of Strang and Walton's patients.[5]

3. Pyrexia is uncommon; when it is present it is generally low grade. The few patients with high fever have thrombophlebitis or cholangitis. Strang and Walton[5] reported that 28 per cent of their cases had an elevation of temperature. This is higher than that seen in most other groups.

4. Abdominal Mass According to Berk,[1] the liver may be palpated in from two-thirds to three-fourths of the patients, although he hastens to add that some of these livers are barely palpable and therefore not necessarily enlarged. Knight and Muether[17] in their series of carcinoma of the pancreas in all locations found hepatomegaly in 67.7 per cent. In Duff's cases[6] of carcinoma of the body and tail there was an incidence of 69 per cent. Strang and Walton[5] noted an incidence of 16 per cent. The hepatomegaly is due to obstruction, metastases, portal vein thrombosis, fatty infiltration.

Berk[1] states that a distended gallbladder can be palpated clinically in about one-half the cases with associated jaundice and in one-third of all cases with or without jaundice. The number of gallbladders found distended at the time of surgery or autopsy is, of course, higher. Malinowski[4] described a distended gallbladder in less than 33 per cent of his patients but he added that at surgery 65 per cent were found to be distended. Knight and Muether[17] found only 14.7 per cent with palpable gallbladders.

Because of the retroperitoneal location of the pancreas, palpation of the primary neoplasm is infrequent. Waugh[28] in fact believes that it is quite rare. Berk[29] noted a pancreatic mass in only 12 per cent of his cases, Knight and Muether[17] in 18.1 per cent, Strang and Walton[5] in 13 per cent, Duff[6] in 2.5 per cent.

Splenomegaly has been described, usually not too frequently. Duff reported an incidence of 25 per cent in his series of carcinoma of the body and tail. The etiology is either portal or splenic vein thrombosis.

5. Ascites may develop due to hepatic or peritoneal metastases, to portal vein thrombosis or portal vein obstruction by enlarged nodes or tumor tissue, or to hypoproteinemia. Berk[1] reported a 15 per cent clinical incidence and a 35 per cent incidence at surgery or autopsy.

Strang and Walton[5] noted that 12 per cent of their patients had ascites, Smith and Albright[22] reported 32 per cent, Brown *et al.*[19] 28 per cent, Knight and Muether[17] 23.8 per cent. In Duff's[6] group 62 per cent of the patients had clinically observed ascites. He believed that ascites is more common in cases of carcinoma of the body and tail than in carcinoma of the head of the pancreas but there are others who disagree with this contention.

6. Superficial Metastases Uncommon—Strang and Walton[5] reported one case that presented with the chief complaint of a painless "lump" in the skin and in another patient it was discovered during the hospital stay.

7. Abdominal Tenderness This was a fairly common finding in Strang and Walton's group, namely 33 per cent incidence.

8. Dilatation of The Superficial Abdominal Veins is occasionally noted. Duff found it in 12.5 per cent, Strang and Walton in 5 per cent. In one of their cases the patient was discovered to have thrombosis of the common iliac veins at autopsy.

9. Abdominal Distention of Moderate Degree Due to Accumulation of Gas in The Intestines has been reported by Strang and Walton in 17 per cent of their series.

10. Virchow's Node not common. Sloan and Wharton[39] stressed the importance, however, of Virchow's node as occasionally being an early finding in carcinoma of the pancreas.

Laboratory Findings [1, 3, 4, 5, 8, 15, 18, 28, 38, 40, 41, 16, 17, 31, 42, 43]

1. Alteration in Carbohydrate Metabolism Berk[1] states that either hyperglycemia or glycosuria or an impaired glucose tolerance curve is present in 40 per cent of patients with primary pancreatic carcinoma. A combination of hyperglycemia, glycosuria and abnormal glucose tolerance curve may be demonstrated in 33 per cent of patients.

In his group at the Graduate Hospital in Philadelphia he found a 78 per cent incidence of an impaired glucose tolerance curve.

In Malinowski's series[4] 71 per cent had an increased fasting blood sugar and 75 per cent had an abnormal glucose tolerance test. Arkin and Weisberg[3] reported an elevated fasting blood sugar in 25 to 50 per cent of cases. Strang and Walton[5] did not find hyperglycemia and glycosuria in their series and glucose tolerance tests were not done.

Burke and Plummer[8] stated that the fasting blood sugar is increased because of functional impairment of acinar cells either from inflammation, edema, or carcinomatous invasion. Brunschwig believed that in a few instances diabetes may result from progressive destruction of the pancreas (D. Cark[15]). Marble, however,[18] is of the opinion that this is rarely the case because of the fairly low incidence of malignancy in the tail where most of the islet tissue is located.

After reviewing the literature on carbohydrate metabolism in non-diabetic patients with carcinoma, he stated that in a large percentage of cases of carcinoma of any type certain slight but definite abnormalities in glucose tolerance curves are noted. Decreased food intake, hepatic metastases, hepatic functional disturbances resulting from prolonged biliary obstruction, and potential diabetes are the factors responsible for abnormal carbohydrate metabolism.

In regard to the increased incidence of carcinomas of the pancreas among diabetics, which was discussed before, Sloan and Wharton[39] reported that 10.2 per cent of their patients had diabetes, most of them for over 4 years.

2. Anemia This is not generally an important feature of this disease, surprisingly, considering the rapid wasting and cachexia. Berk[1] reports an incidence of 33 per cent, usually of mild degree. Clark,[15] however, found that 61 per cent of his patients were anemic, Malinowski[4] noted 60 per cent, Strang and Walton[5] 45 per cent, Burke and Plummer[8] only 26 per cent.

3. White Blood Count This varies widely. In 30 per cent of Strang and Walton's series there was a leukocytosis. The importance of leukocytosis was stressed by Brown *et al.*[16] and by Arkin and Weisberg,[3] who noted that it is usually seen in patients with metastases.

4. Blood in The Stools About 25 per cent of patients show occult blood in the stools, according to Berk.[1] Malinowski found that 43 per cent of his group showed occult blood, which was not due to hypoprothrombinemia because most of the patients had prothrombin times above the critical level. It is due, usually, to the oozing of malignant tissue which has invaded the gastrointestinal tract or to destructive changes of adjacent tissue and blood vessels. Gross bleeding is not too common but as discussed before, does occur, due to malignant invasion of the gastrointestinal tract with secondary ulceration, hypoprothrombinemia, and fibrinogenopenia.

5. Steatorrhea Large, bulky, fatty stools are rare in carcinoma of the pancreas. They are more likely to be seen in carcinoma of the head. Berk[1] found an incidence of only 4 per cent in the patients studied at the Graduate Hospital in Philadelphia. Some place the incidence as high as 10 per cent.

6. Creatorrhea The constant finding of large numbers of undigested muscle fibers in the stools is diagnostic of some disease of the pancreas. The loss of nitrogen in the feces is also of some importance. Normally the maximum loss is 15 per cent. In pancreatic obstruction the average loss is 40 per cent.

7. Liver Chemistries The elevated icterus index and serum bilirubin have been discussed before. Malinowski[1] reported an increased alkaline phosphatase in 92 per cent of his cases, an abnormal liver profile, including hypoproteinemia and reversal of the A/G ratio in 69 per cent. When one considers that these patients often have long-standing jaundice, the biliary hepatitis or cirrhosis that results is understandable. He also found a hypoprothrombinemia in 53 per cent. Burke and Plummer[9] found that 37 per cent of their cases had an increase in alkaline phosphatase. Knight and Muether[11] believe that there is little correlation between the alkaline phosphatase, degree of bilirubin retention, site of involvement, or presence of metastatic lesions. In their series 42.4 per cent had an elevated serum cholesterol and most had normal serum proteins. Sloan and Wharton[10] observed hypoproteinemia in 31 per cent of their cases; it was most marked in those patients whose malignancy involved the head alone. The hypoproteinemia is due to failure in digestion and absorption of ingested protein, loss of protein in ascites and edematous tissues, hemorrhage, hepatic disturbance and priority for nitrogen that rapidly growing malignant tumors possess.

8. Urobilinogen Excretion The amount of urobilinogen in the feces and urine varies with the completeness of the obstruction, if present.

9. Bilirubinuria This is likewise dependent upon obstruction of the biliary passages.

10. Serum Amylase and Lipase Most authors agree that there is some value to these determinations if they are repeated in serial fashion. In the early stages, as the neoplasm obstructs the pancreatic ducts, the serum enzymatic concentration rises. As the pancreatic tissue becomes increasingly destroyed, the production of enzymes decreases and their concentration in the peripheral blood falls, often to subnormal levels. Comfort and Osterberg[10] found an elevated serum lipase in the early stages of carcinoma of the pancreas in 40 per cent of their cases and an elevated serum amylase in only 8 per cent.

Doubilet *et al.*[38] however, did not find an increase in serum lipase unless there was also an increase in serum amylase.

Berk[3] noted a hyperlipasemia in over one-third of his cases prior to surgery and in almost two-thirds at some stage of the disease. Ross and Klinge[41] reported that random serum amylase determinations are elevated in one-third of cases of carcinoma of the head. Burke and Plummer[9] found that, on one determination, 17 per cent of the patients had an elevated serum amylase and 17 per cent had decreased values. Knight and Muether[17] stated that 65 per cent of their group had either an increase or a decrease in serum amylase, depending upon the stage of the malignancy.

11. Duodenal Drainage Following the administration of secretin or mecholyl, there is a release of external pancreatic secretion into the duodenum if the pancreatic ducts are open. Ross[34] stated that in over 90 per cent of the cases in which carcinoma is in the head of the pancreas abnormalities will be noted. The commonest are diminished concentration of one or more of the enzymes, reduction in total volume of secretion, and lessened concentration of bicarbonate.

The normal volume range following stimulation with secretin is 2 to 4.5 cc./kg. body weight, the maximum bicarbonate concentration about 90 to 125 mEq./L., and the total amylase after 30 minutes is 450 to 1300 Somogyi units, according to tests performed by Dreiling and Hollander.[42] The wide range exhibited by the amylase would seem to take it out of the realm of usefulness as a test for pancreatic function.

Duodenal drainage also may yield blood cells; this is highly suggestive of malignancy. McNeer and Ewing[43] found carcinoma cells in the duodenal drainage of some cases of carcinoma of the pancreas.

Gastroscopy Findings Gastric defects may be produced by underlying pancreatic neoplasms and be visible as a bulging into the stomach wall or a rigidity of a portion of the wall upon gastroscopic examination.

Peritoneoscopy The pancreas cannot be visualized through the peritoneoscope because of its deep retroperitoneal location. Peritoneoscopy, however, may prove of value in identifying other lesions with which carcinoma of the pancreas may be confused, in observing metastases, and in localizing the primary site of a neoplasm by biopsy.

Radiological Manifestations [44, 45, 46, 47, 1, 2, 4, 5, 10] Definite x-ray evidence of carcinoma of the pancreas usually is not observed until the neoplasm is quite large. In the early stages, however, one or more suggestive signs often make their appearance and these in conjunction with the history and clinical picture may lead one to suspect the presence of a malignancy.

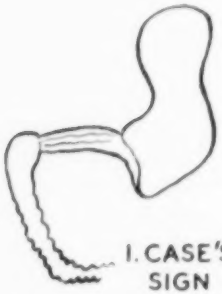
Hodes *et al.*,[44] in a review of 105 cases of carcinoma of the head of the pancreas, stated that about 50 per cent of the tumors were not recognized by them on x-ray. When they reviewed the initial x-rays of these 50 per cent after the diagnosis had been made at surgery or autopsy or from x-rays taken in the late stages of the disease, they decided that in almost all cases the correct diagnosis could have been made from the original studies.

Hodes *et al.* and Beeler and Kirklin[45] hold that there exists no significant relation between the size of the

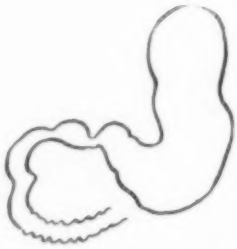
pancreatic neoplasms and their ease of demonstration roentgenographically.

Recognition of the tumors depends upon their ability to distort either by pressure or actual invasion of the barium filled viscera that surround them. Needless to say, carcinoma of the head is more likely to manifest itself in this manner than carcinoma of the body or tail.

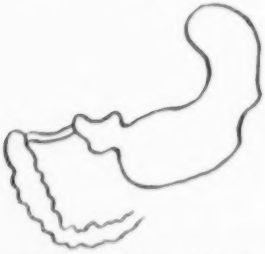
Stomach The pylorus and antrum are the portions of the stomach usually affected. They may be displaced upward or downward as well as forward. This can be noted best in the supine position.



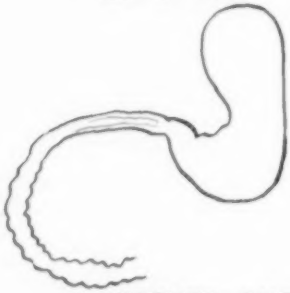
1. CASE'S PAD SIGN



2. FROSTBERG'S INVERTED "3" SIGN

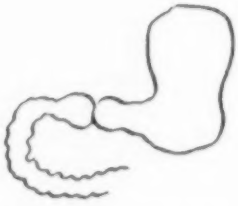


3. POST-BULBAR DUODENAL IMPRESSION DUE TO DILATED COMMON DUCT



4. WIDENED DUODENAL SWEEP

5. PRESSURE DEFECT CAUSED BY A CA OF THE HEAD



6. DIVERTICULUM IS DISPLACED UPWARDS

In 1940 Case[46] described his "pad" sign which has since been considered highly significant of neoplasms in the head of the pancreas. It is a circumscribed filling defect in the gastric silhouette due to pressure by the tumor, which may be noted in the horizontal position and may disappear completely in the erect position. Carefully guided palpation may, however, reproduce this finding in the erect position.

Retrogastric soft tissue space enlargement may displace the stomach or duodenum, usually anteriorly. According to Gottlieb *et al.*[47] this is often an early sign and one that may escape detection on routine G.I. series. Lateral radiography, including exposures in the upright and recumbent position, significantly increases the likelihood of recognizing this abnormality. In Hodes' group of cases, however, retrogastric displacement was an unusual finding.

Infiltration of the stomach wall with ulceration may lead to an erroneous diagnosis of gastric ulcer.

According to Case there is a tendency in patients with carcinoma in the head of the pancreas to rapid emptying of the stomach, suggesting achylia. This may be observed on fluoroscopy.

Duodenal Bulb The "pad" effect may be seen in the duodenum as well as in the stomach. The bulb may be pushed up, down, or forward, depending upon the location of the neoplasm. Occasionally the bulb may be distorted by a dilated common duct. This more commonly affects the post-bulbar portion of the duodenum, however. Rapid filling of the bulb with delayed emptying and arrhythmic and irregular contractions of the bulb have been noted. Infiltration of the bulb or pressure from a dilated common duct may produce patterns suggestive of an ulcer. This may be especially confusing if the patient has ulcer-type pain with relief by food or alkalies. Berk[1] stated that 12 per cent of patients have complaints resembling those of peptic ulcer and Beeler and Kirklin found a 14 per cent incidence of supposed duodenal ulcer diagnosed on x-rays of a group of proven cases of carcinoma of the pancreas.

Descending Duodenum Wide duodenal loops with major duodenal displacement are not very common, according to Hodes. One is more likely to note normal or minimally distorted loops. In 1938 Frostberg described the inverted "3" sign of the medial border of the descending limb due to pressure effects from carcinoma of the head. However, infection and edema of the pancreas can also cause it. Generally, the inverted "3" can be seen best in the supine position and often is seen only in that position.

At times a dilated gallbladder may produce a pressure defect upon the duodenal bulb or descending duodenum. This takes the form of a curve with its concavity facing the distended gallbladder. More striking and important is the pressure defect caused by a dilated common duct ("duodenal impression"). This can be noted most advantageously in the prone right anterior oblique or prone right lateral positions. Usually its appearance suggests a narrowing of the duodenum and an abrupt change in its course. Generally, it lies in the immediate post-bulbar region.

Disordered motor function in the descending limb of the duodenum may often be noted during fluoroscopy. Normally, peristalsis in this area is even

and symmetrical. Limited or even a lack of peristalsis may be observed, most frequently along the medial border of the duodenal loop.

Furthermore, infiltration of the duodenum may cause abnormalities of the duodenal folds, especially along the medial border. If diverticula arise in this region, they may be displaced, which is a very significant finding.

Partial or even total duodenal obstruction may occur.

Occasionally, the medial aspect of the duodenal loop assumes a double contour or profile. Whether this is due to invasion plus pressure by the mass or to some other cause, the medial border of the loop seems reduplicated.

Hodes *et al.* described a peculiar finding noted in prone films taken in a true postero-anterior projection. The duodenal loop, instead of curving, seemed straight and was superimposed on the shadows cast by the duodenal bulb and the pylorus. This was produced by the combined effects of medial displacement of the descending duodenum and infiltration.

Burke and Plummer[9] noted calcifications in the pancreas in one of their cases of carcinoma with a past history of recurrent pancreatitis.

Malinowski[4] reported that 55 per cent of his group with carcinoma of the pancreas had either pressure deformities of the duodenum and widening or displacement of the duodenal loop or pressure defects of the pyloric antrum. Strang and Walton[5] found abnormal G.I. series in 53 per cent of their cases of carcinoma of the body and tail but in only 20 per cent was the abnormality really suggestive of pancreatic neoplasm (namely, a mass producing a filling defect in the stomach but apparently arising behind the organ). The findings in the other 33 per cent were duodenal cap deformity, "ulcer crater" on the lesser curvature of the stomach and esophageal obstruction. Brown *et al.*[10] noted abnormal G.I. series in only 28 per cent of their cases of pancreatic carcinoma.

Treatment and Prognosis [48, 49, 50, 34, 51, 52, 53, 54, 55, 12, 8, 56, 57] The treatment is surgical but the prognosis is poor. Because of the indefinite nature of the early symptoms due, primarily, to the location of the pancreas, patients usually present themselves or are diagnosed too late for any procedure other than a palliative one.

The simplest of all palliative procedures to relieve jaundice is the insertion of a T-tube but this technic has the disadvantages of loss of electrolytes and water and the problem of continual external drainage. If this method must be adopted, however, the situation is improved by inserting an enterostomy tube which then can be connected to the T-tube externally, allowing bile to be returned to the intestine.

Choledochojejunostomy, cholecystoduodenostomy, and cholecystojejunostomy are the more preferable palliative procedures.

In 1935 Whipple[48] reported a successful two-stage operation for carcinoma of the ampulla of Vater. This has since been employed in patients with early carcinoma of the head of the pancreas. One of the deterring factors in the development of radical surgery for such lesions was the belief that pancreatic secretions were necessary to life. However, it has been proven that normal digestion does occur and that complete exclusion of pancreatic secretions from the gastrointestinal tract is com-

patible with good health.

The work of Whipple,[48] Child,[49] Brunschwig,[50] and others has resulted in standardization of surgical technic which permits block dissection of the head of the pancreas, duodenum, and distal portion of the common duct. Then the continuity of the gastrointestinal tract is restored by closing the severed proximal end of the jejunum and performing a gastrojejunostomy. The pancreatic ducts (if possible) and the common bile duct are anastomosed to the jejunum proximal to the gastrojejunostomy.

While many surgeons subscribe to Whipple's subtotal pancreatectomy in operable cases of carcinoma of the head, there are others who believe that anything less than total pancreatectomy is useless. Ross[34] stated that besides total pancreatectomy surgery should include cholecystectomy and resection of the common duct with its lymph nodes, areolar tissue, and nerve fibers, a high gastric resection to remove the maximum of lymph drainage and to guard against gastrojejunal ulcer, resection of the spleen, all of the duodenum, and the areolar tissue and nodes along the hepatic, coeliac, and left gastric arteries. He did not find that total pancreatectomy added to the operative mortality.

Child *et al.*[51] recently reported several successful attempts at both total pancreatectomy and resection of the portal vein.

It is still too early to determine whether total pancreatectomy will result in more 5 year survivals.

Morel *et al.*[52] discussed the physiological changes produced by pancreaticoduodenectomy. The isles of Langerhans, as noted before, are located mainly in the tail of the pancreas. Therefore, only a small portion of the gland need be preserved to supply sufficient insulin for glucose metabolism. If total pancreatectomy is performed, most patients can be maintained on 20 to 30 U. of insulin a day, as determined by Warren.[53]

If the pancreatic ducts are ligated or there is total excision of the pancreas, the stool will temporarily be bulky, soft, and grey due to incomplete digestion and absorption of fats. This diarrhea may be relieved by taking pancreatin. This is usually necessary for only a few months because eventually the functions of the pancreatic juice are taken over by other digestive secretions.

The status of lipocaic, or pancreatic hormone, has not been fully determined. Fatty infiltration of the liver may result from its absence, according to some reports. However, observations on the presence of fatty infiltration of the liver in autopsied patients following pancreatectomy have been inconclusive. Rosenberg[54] reported a case of fatty metamorphosis of the liver in a diabetic patient that responded well to treatment with lipocaic. Choline and methionine will prevent such changes.

Radical procedures for carcinoma of the body or tail of the pancreas are rarely possible because of the usual finding of metastases at the time of surgery.

The operative mortality in the first 10 years after Whipple introduced his radical technic was between 30 and 40 per cent. This has been steadily lowered. Ross had only one operative mortality in his last 9 cases prior to his article published in 1954. More recent series report between 10 and 15 per cent. Cattell and Warren[55] report 12.7

per cent. However, Moore and Younghusband[12] in their report (1954) listed an operative mortality of 38 per cent.

The long range viewpoint has been very discouraging. Few patients have survived the arbitrary 5 year period. Miller[8] stated that 10 per cent of his cases were alive after 5 years. In a survey by Logan and Kleinsasser[58] of all cases of pancreaticoduodenal resections for malignancy reported in the literature between April 1942 and June 1949, among 30 cases of carcinoma of the pancreas followed for 5 years there was 1 survival (or 3 per cent).

Statistics of Cattell and Warren[59] concerning their cases of carcinoma of the head of the pancreas are equally unfavorable, namely, 1 survival out of 18, or 5.5 per cent.

The average length of survival after palliative procedures is 9 months. Cattell and Pyrtek[57] reported that the average survival after successful radical surgery is 11 months. Since the untreated case survives, on the whole about 6 to 8 months, the conclusion must be reached that surgery at this time has no more to offer for this disease than the relief of jaundice.

Therefore until earlier diagnosis by means of a high index of suspicion, employment of pertinent laboratory procedures, painstaking roentgenologic technics, and exploratory laparotomies in bizarre cases is accomplished, the survival statistics will continue to be unfavorable.

Summary

Primary carcinoma of the pancreas has been discussed. It is most common in males between the ages of 50 and 60. Approximately three times as many malignancies occur in the head as in the body and tail.

Several possible etiologic factors have been presented including developmental errors, aberrant pancreatic tissue, chronic pancreatitis, chronic cholecystitis, alcoholism, diabetes mellitus, food, food products, and dietary habits.

The histologic type is usually the cylindric-cell adenocarcinoma. Venous thrombosis is commonly associated with carcinoma of the pancreas, especially of the body and tail.

It is characterized mainly by abdominal and back pains, jaundice, marked weight loss, anorexia, various gastrointestinal complaints, and weakness. The chief physical signs are icterus, emaciation, abdominal mass (usually hepatomegaly), and ascites.

Hyperglycemia, glycosuria, abnormal glucose tolerance curve, disturbed liver chemistries, increased or decreased serum amylase and lipase, and duodenal drainage abnormalities are some of the pertinent laboratory findings.

The radiologic manifestations are defined and a discussion of treatment and prognosis included.

Bibliography

1. Berk, J. E. in Bockus' Gastroenterology Vol. III:807 W. B. Saunders Co., Philadelphia. 1946.

2. Hick, F. K., and Mortimer, H. M.: Carcinoma of the pancreas. J. Lab. and Clin. Med. 19:1058. 1934.

3. Arkin, A., and Weisberg, G.: Carcinoma of the pancreas, a clinical and pathological study of seventy-five cases. Gastroenterology 13:118. 1949.

4. Malinowski, T. S.: Clinical observations on pancreatic malignancies. J. Indiana M. Assoc. 46:25. 1953.

5. Strang, C., and Walton, J. N.: Carcinoma of body and tail of pancreas. Ann. Int. M. 39:15. 1953.

6. Duff, G. L.: Carcinoma of body and tail of pancreas. Bull. Johns Hopkins Hosp. 65:69. 1939.

7. Mishkarek, P. A.: Case reports of carcinoma of the pancreas. Ann. J. Path. 11:527. 1935.

8. Miller, E. M. et al.: Carcinoma in the region of Ampulla of Vater. Surg. Gynec. and Obst. 92:172. 1951.

9. Burke, J. O. and Plummer, K.: Carcinoma of the pancreas. Virginia M. Month. 80:333. 1953.

10. Brown, P. K., Moseley, V., Pratt, T. D., and Pratt, J. H.: The early diagnosis of cancer of the pancreas based on the clinical and pathological study of one hundred autopsied cases. Am. J. M.Sc. 223:349. 1952.

11. Thompson, C. M., and Rodgers, L. R.: Analysis of the autopsy records of 157 cases of carcinoma of the pancreas with particular reference to the incidence of thromboembolism. Am. J. M. Sc. 223:469. 1952.

12. Moore, R. G. and Younghusband, J. D.: Carcinoma of the head of the pancreas. Brit. J. Surg. 41:562. 1954.

13. Clark, D. H.: Carcinoma of the pancreas. North Carolina M. J. 14:210. 1953.

14. Grauer, F. W.: Pancreatic carcinoma: Review of 34 autopsies Arch. Int. Med. 63:884. 1939.

15. Ewing, J.: Neoplastic Diseases. 4th Ed. Phila., W. B. Saunders Co., 1940.

16. Doubilet, H. et al.: The diagnosis of biliary pancreatic carcinoma. Surg. Cl. N. Amer. 33:461. 1953.

17. Knight, W. A. and Muether, R. O.: Carcinoma of the Pancreas. Southern M. J. 46:660. 1953.

18. Ullin, A. W. et al.: Carcinoma of the gall bladder. Gastroent. 15:684. 1950.

19. Marble, A.: Diabetes and cancer. New England J. Med. 211:339. 1934.

20. Sproul, E. E.: Carcinoma and venous thrombosis: Frequency of association of Carcinoma in body and tail of pancreas with multiple venous thrombosis. Am. J. Cancer 34:566. 1938.

21. Kenney, W. E.: The association of carcinoma in the body and tail of the pancreas with multiple venous thrombi. Surgery 14:600. 1943.

22. Wright, I. S.: The pathogenesis and treatment of thrombosis. Circulation. 5:161. 1952.

23. Leach, W. B.: Carcinoma of the pancreas. A clinical and pathologic analysis of thirty-nine autopsied cases. Am. J. Path. 26:333. 1950.

24. Miller, J. R., Baggenstoss, A. H., and Comfort, M. W.: Carcinoma of the pancreas. Effect of histological type and grade of malignancy on its behavior. Cancer 4:233. 1951.

25. Jennings, W. K. and Russell, W. O.: Phlebothrombosis associated with mucin-producing carcinomas of the tail and body of the pancreas. A clinicopathologic study of two cases with necropsy. Arch. Surg. 56:186. 1948.

26. Gore, I.: Thrombosis and pancreatic carcinoma. Am. J. Path. 29:1093. 1953.

27. Innerfield, I., Angrist, A., and Benjamin J. W.: The antithrombin titer in acute pancreatitis. Bull. New York Acad. Med. 27:399. 1951.

28. McKay, D. G., Mansell, H., and Hertig, A. T.: Carcinoma of the body of the pancreas with fibrin thrombosis and fibrinogenopenia. Cancer 6:862. 1953.

29. Berk, J. E.: Diagnosis of carcinoma of the pancreas. Arch. Int. Med. 68:525. 1941.

30. Rothenberg, R. E., and Aronson, S. G.: Acute cholecystitis preceding neoplastic common bile duct obstruction. Ann. Surg. 112:400. 1940.

31. Narsun, F. M.: An unusual case of carcinoma of the head of the pancreas. Brit. J. Surg. 41:439. 1954.

32. Smith, B. K. and Albright, E. C.: Carcinoma of the body and tail of the pancreas; report of 37 cases studied at the State of Wisconsin General Hospital from 1925-1950. Ann. Int. Med. 36:90. 1952.

33. Bliss, W. R., Burch, B., Martin, M. M., and Zollinger, R. M.: Localization of referred pancreatic pain induced by electric stimulation. Gastroenterology 16:317. 1950.

34. Ross, E. E.: Carcinoma of the pancreas. Am. J. Surg. 87:20. 1954.

35. Rancom, H. K.: Carcinoma of pancreas and extrahepatic bile ducts. Am. J. Surg. 40: 264. 1938.

36. Yaskin, J. C.: Nervous symptoms as earliest manifestations of carcinoma of the pancreas. J.A.M.A. 96:1664. 1931.

37. Ullatt, G. and Parsons, E. H.: Psychiatric aspects of carcinoma of the pancreas. J. Missouri M. A. 45:490. 1948.

38. Waugh, J. M.: Radical resection of the head of the pancreas and total pancreatectomy. J.A.M.A. 137:141. 1948.

39. Sloan, L. E. and Wharton, G. K.: Carcinoma of the pancreas. Am. J. Gastroent. 21:441. 1954.

40. Comfort, M. W. and Osterberg, A. E.: Serum amylase and serum lipase in diagnosis of disease of pancreas. M. Clin. North America 24:1137, 1940.

41. Ross, C. A. and Klinge, F. W.: Pain and hyperamylasemia as an early sign of carcinoma of the head of the pancreas and of the ampulla of Vater. Gastroent. 12:204, 1949.

42. Dreiling, D. A., and Hollander, F.: Studies in pancreatic function. Gastroent. 15:620, 1950.

43. McNeer, G. and Ewing, J. H.: Exfoliated pancreatic carcinoma cells in duodenal drainage. Cancer 2:643, 1949.

44. Hodes, P. J. et al.: Pancreatic, ductal, and vaterian neoplasms: their roentgen manifestations. Radiology 62:1, 1954.

45. Beeler, J. W. and Kirklin, B. R.: Roentgenologic findings accompanying carcinoma of the pancreas. Am. J. Roentgenol. 67:576, 1952.

46. Case, J. T.: Roent. pan. dis. Am. J. Roentgenol 44:485, 1950.

47. Gottlieb, C. et al.: Bulbar defects in pancreatic neoplasm resembling duodenal ulcer. Gastroent. 23:82, 1953.

48. Whipple, A. O. et al.: Treatment of carcinoma of the ampulla of Vater. Ann. Surg. 102:763, 1935.

49. Child, C. G.: Newer concepts in surgery of the pancreas. Med. Ann. District of Columbia 19:1, 1950.

50. Brunschwig, A.: Surgical therapy of carcinoma of the pancreas. J. Kansas M. Soc. 50:25, 1949.

51. Child, C. G.: Pancreaticoduodenectomy with resection of the portal vein in the macaca mulatta monkey and in man. Surg. Gynec. and Obst. 94:31, 1952.

52. Moreil, E. L.: Pancreaticoduodenal resection. Am. J. Gastroent. 21:435, 1954.

53. Warren, K. W.: Some aspects of total pancreatectomy. Lahey Clinical Bulletin 7:86, 1941.

54. Rosenberg, D. H.: Proved case of recovery from fatty metamorphosis of liver after treatment with lipocaic. Am. J. Digest. Dis. 5:607, 1938.

55. Cattell, R. B., and Warren, K. W.: Surgery of the Pancreas. W. B. Saunders Co., Philadelphia, 1953.

56. Logan, P. B. and Kleinsasser, L. J.: Surgery of the pancreas. Internat. Abstracts Surg. 93:521, 1951.

57. Cattell, R. B. and Pyrtek, L. J.: Appraisal of pancreaticoduodenal resection. Ann. Surg. 129:840, 1949.

AN EXERCISE IN DIAGNOSIS— THE CASE REPORTS

IN addition to our regular quota of original articles, "Refresher" articles and departments, this issue, and every issue, contains selected Case Reports from the Clinico-Pathological Conferences at New York University-Bellevue Medical Center. You will find them on pages 937-942. We recommend these studies as interesting and stimulating.

Anesthesiology and the Law

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The modern anesthesiologist is a vital participant in the total treatment of the patient who requires his services. He knows the state of the circulation during the anesthetic procedure by means of the Sphygmomanometer, the Oscillometer, and the Electrocardiograph. The oxygen saturation of the blood is indicated to him by means of the Oximeter. The patient's response to surgical stimuli can now be interpreted by means of the Electroencephalogram.

By means of the technique of induced hypotension which reduces hemorrhage bloodless fields of operation are now possible in brain, plastic and abdominal surgery. By means of the use of hypothermia (cold in the extreme degree) procedures in complicated cancer surgery are being carried out painlessly. Further, since extreme cold causes diminution of the cardiac inflow, operations on the heart are being performed under direct vision. In poor cardiac risk patients a new technique has been evolved whereby intra-cardiac surgery may be performed. Less burden is placed on their cardio-vascular systems because they are operated upon in the first stage of ether-oxygen anesthesia. Analgesia is produced with the patient kept conscious during the procedure, for which a total amnesia results.[1]

The modern, qualified anesthesiologist is a physician of broad background. He interprets and integrates laboratory findings. He suggests to the surgeon the proper form of anesthesia in the light of the existing pathology and the nature of the intended surgical procedure. Even though the surgeon has examined his patient pre-operatively, the anesthetist does so pre-anesthetically. He analyses previous illnesses, anesthesias and allergies. He re-evaluates by means of physical examination the patient's

cardiac, respiratory and nervous systems. He may need roentgenological or electrocardiographic study. He observes the nutritional state of the patient and he learns of the presence of anemia. He gets an idea of the electrolyte and water balance; the state of the liver and kidneys and possibly the presence of any foci of infection. He makes a note of the state of the superficial veins and prepares for tranfusion if necessary. He prescribes the pre-anesthetic medication and makes certain that the patient's stomach is empty before the procedure begins.

It is then his duty to produce the proper depth of anesthesia and maintain it as long as it is required. He records the blood pressure, pulse and respiration and keeps oxygen available. If tracheobronchial aspiration is indicated he uses it. If artificial respiration or a special drug is needed he administers it. Only when the patient has become self-sustaining, all signs of labored breathing or cyanosis have passed, and the patient has fully reacted, is the anesthesia considered to have been concluded.

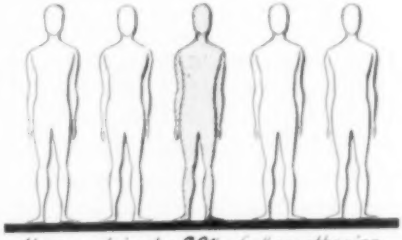
Not only in surgery, but in many other realms, is anesthesia being utilized in the physician's armamentarium. In mental disease, anesthesia is being used more and more as an adjunct in the diagnosis and treatment of patients. Therapeutic nerve block is used in the treatment of certain paresthesias where surgery is contra-indicated. Newer diagnostic technics (e.g. translumbar aortography) have been made possible because of anesthesia.

The preceding account is given to indicate why there are some 8 million anesthesias administered yearly in the United States. Beecher and Todd[2] studied deaths associated with anesthesia in a series of 599,548 cases and pointed out the following revealing statistics:

(1) Approximately eight million anesthesias are administered in all hospitals in the United States each year. This was the number administered to a population of one hundred and fifty-six million people.

(2) Deaths attributable to anesthesia were 3.29 per hundred thousand population. By comparison there were only 1.38 deaths per hundred thousand population due to poliomyelitis. *Thus, there are twice the number of deaths from anesthesias as there are from poliomyelitis each year.*

(3) Out of each 1,560 anesthesias there is one death attributable to the procedure.



Nurses administer 20% of all anesthesias

(4) Of all primary inhalation anesthesias in use from the statistics collected in ten university hospitals, ether was used in 62% of the cases.

(5) Nurses administer 20% of all anesthesias. Nurses account for twice as many anesthesias as physician specialist anesthetists.

The modern anesthetist must pay special attention to the condition of the apparatus that he uses. Obvious sources

of ignition from electric power sparks, arcs in open motors, switches, receptacles, exposed incandescent wires and hot-plates must be eliminated. Most anesthetic gases are combustible and mixtures of these with air, nitrous oxide or pure oxygen may be explosive. When an explosion occurs in the area of the anesthesia it may be the result of the careless use of flames, electro-cautery, and high frequency coagulating and cauterizing apparatus. Sparks are sometimes initiated by defective electrical equipment. The accidental mixing of oxygen with combustible gases at high pressures has caused explosion. The use of lubricating oils on oxygen valves and regulators has been described as the cause of accidental explosion. The most common cause of fires and explosions in the operating room is static electricity.[3]

In a court case, the plaintiff sought to "recover" for the death of a relative which occurred during an operation, when the anesthetic gases being administered exploded. Judgment for the plaintiff was reversed and a new trial ordered since the jury was improperly permitted to draw the inference that the explosion would not have occurred had proper safeguards been adopted. It was a prejudicial error to permit the cross-examination of a witness with reference to a professional article which stated that none of the 63 static fires referred to therein occurred under a set-up which was regarded as offering maximum protection.[3a]

Standard of Care A physician, surgeon or dentist is not required to exercise the highest degree of skill and care possible in the treatment of the patient, but generally is duty-bound to exercise only the degree of skill ordinarily employed under similar circumstances by members of his profession in good standing in the same locality and to use reasonable care and diligence and his best judgment in application of his skill to a particular case.[4]

Before a physician or surgeon can be held liable for malpractice, he must have done something in the treatment of his patient which the recognized standard of medical practice in his community forbids in such case, or he must have neglected to do something required by those standards.[5]

In another court case[6] it was pointed out that only with difficulty could the patient be relaxed. As the anesthesia was being administered the patient had become more and more cyanotic. To relieve the cyanosis the mask was raised and the anesthesia was continued for forty-five minutes longer. The patient died.

It was held that if a surgeon persists in the use of an anesthetic after a warning which would impel one of reasonable prudence to desist, he should be answerable for the consequences. In this case, no expert testimony was necessary.

Consent Everyone has a right to determine what shall be done to his body while he is alive.[7] Consent for anesthesia must be given by an adult who is in a clear state of mind and who gives it "understandingly". Consent is best when it is specific, but is sufficient when applied to "any and all forms of anesthesia".

The consent of a person of unsound mind is no consent in law. In the case of a minor, consent must be obtained from the parent or guardian. However, in the presence of an absolute emergency the law presumes "constructive consent" to do what is necessary to save life.

Physician Anesthetist An anesthetist who is a physician and qualified to administer anesthesia is not the surgeon's agent when he administers an anesthetic to a patient.[9] As example, a surgeon's agreement with a patient that she would not be given a spinal block meant that the surgeon would do everything that could be reasonably expected of him to see that she was not given one. However, the surgeon was not an insurer. He did everything that he was obliged to do by making notation on the hospital chart which he intended that the anesthetist would read. The anesthetist did read this notation, but administered spinal block anyway. Therefore the surgeon was not liable for injuries allegedly resulting from the spinal block.[9]

The anesthetist who has no part in the control of the operation is not liable for the negligence, if any, of the operating surgeon. The physician anesthetist who is qualified in anesthesia acts as an independent contractor when he administers an anesthetic over which he has total control.

The Nurse Anesthetist Anyone who who is not a licensed physician who administers anesthesia must do so under supervision. Although she may be qualified by training in an accredited school of anesthesia and has qualified for admittance to the American Association of Nurse Anesthetists, she would be engaged in the practice of medicine unless she were supervised in the administration of anesthesia by a physician. She may be in the employ either of the hospital or the physician, either of whom may be liable as her employer. The fact that the employer is liable does not mean that she is not. In many cases where both the hospital and nurse are liable, the patient might choose to enforce the liability of the hospital. The escape from liability in such a case is because of the choice of the patient, not because the liability did not exist. Every case is decided on the basis of whether or not the nurse was negligent.[10]

The question that must be answered is: did she or did she not breach the duty which the law imposes upon her? The jury must decide this issue of fact. Expert testimony supplies the information as to what is proper.

Where a nurse follows the instructions of a physician she is under his control. It is this element of control which protects her unless the order she received from the physician was clearly unreasonable. The nurse is not expected to exercise judgment. She will use the equipment which is furnished to her by the hospital and is thereby protected unless there is something to indicate to her that this equipment is defective.

In an action against a hospital and doctor for injuries sustained during administration of an anesthetic where the issue was whether the nurse anesthetist was the agent of the doctor or the hospital, testimony that it was customary for surgeons to rely entirely upon nurse-anesthetists was admissible even though

the doctor had not pleaded such custom as a defense.[11]

When a surgeon occupies such position his duties and liabilities respecting supervision and control over administration of the anesthetic are substantially the same as those respecting the phases of the operation and treatment of the patient generally. He is bound to exercise such reasonable care and skill respecting the administration of the anesthetic as is usually exercised by average physicians and surgeons in the same community.[12]

It is true that the nurse was in the employ of the hospital. Nevertheless on the record it can be inferred that she stood in the position of a "lent servant" who for the purposes and duration of the operation occupied the position of a servant of the doctor. The rule is: where a servant has two masters, a general and a special one, the latter, if having the power of immediate direction and control, is the one responsible for the servant's negligence.

When anesthesia is administered by a nurse in the employ of a hospital or any other person, except a licensed physician, the operating physician assumes the liability for negligence if there is any.

Whether the physician exercieses it or not, it is his right of control which may be the deciding factor on the issue of his liability. Whenever acts are carried out by persons in the employ of the hospital but under the supervision and control of the physician then he becomes responsible for their acts. The physician, however, has the right to expect that the nurses employed by the hospital have had adequate training. If she should prove to be incompetent, then the physician would be freed of liability unless he knew, or had reason to know that she was incompetent.

Proximate Cause In a malpractice action for lung abscesses allegedly resulting from aspiration of foreign material from the mouth following extraction of teeth by a dentist while a patient was under general anesthesia, the patient failed as a matter of law, to establish the element of proximate cause.[14]

To recover for the death of a patient whose death was allegedly caused by the use of Pontocaine solution in a nasal spray, evidence was insufficient to establish that the death of the patient was caused by use of Pontocaine solution.[15]

Most drug reactions are encountered with local anesthetics.[15a] The stimulation of the central nervous system or depression of the vascular system are the mechanisms involved when the blood level exceeds a certain threshold of local anesthesia. The stimulation of the central nervous system may result in excitement, tachycardia, nausea, vomiting, and convulsions. Larger doses still may depress the nervous system and cause paralysis or a coma-like state. The vascular reaction may manifest itself either in depression of the myocardium, or widespread vaso-dilatation, or both. When the latter occurs, severe circulatory collapse may result.

Allergy has been blamed for these reactions when in reality they are usually due to over-dosage. The anaphylactic reaction which is characterized by sudden syncope after the injection of minute amounts of local anesthetic drug occurs but rarely. The allergic manifestation of antigen-antibody type takes place after repeated exposures to local anesthetic drugs. Doctors and dentists are prone to this type of reaction which is manifested by exzema of the hands;

urticaria; edema of eyelids and sneezing.

The physician will do well to prescribe a barbiturate before administering a local anesthetic. Also, the avoidance of over-dosage especially in vascular areas will act as a deterrent to the train of symptoms known as a "reaction".

Expert Testimony In an action against a surgeon for alleged malpractice in allowing a breathing tube to become lodged in the plaintiff's throat, and failing to discover its presence for about 36 hours after an abdominal operation upon her, professional and non-professional testimony was sufficient to sustain a jury's verdict for the plaintiff.[16]

Only in a case where there is manifest such obvious gross lack of care or skill on the part of the physician as to afford of itself an almost conclusive inference of lack of care, is testimony of expert witnesses not necessary in a malpractice action.[15]

In a malpractice suit against two osteopathic physicians and an anesthetist for improperly administering a spinal anesthetic whereby the plaintiff's lower extremities were paralyzed, physicians of either osteopathic or medical schools, both of which use the same method of administering spinal anesthesia, were qualified to testify as to the anesthetist's specific acts in administering spinal plaintiff's paralysis could be proved only block.

However, proximate cause of the by expert witnesses of the osteopathic school of practice.[17]

Res Ipsa Loquitur When a patient suffers injury to some part of the body not under surgery during anesthesia there is a presumption of negligence on the part of those in control of the patient's body or the instrumentality causing the injury.[18]

Where the circumstances of the injury provide reasonable inference that if due care had been employed, the untoward reaction would not have happened, negligence may fairly be inferred in the absence of any explanation.[19]

The doctrine of res ipsa loquitur does not prevail where the party against whom it might apply accepts the duty of going on with the proof and details of the entire transaction. In such a situation, the presumption, inference, or doctrine ceases to exist and all questions concerning the injury must be determined from the evidence.[20, 21]

Summary

1. During 1953 out of 8,000,000 anesthesias that were administered there were 5128 deaths attributable to the anesthesia. This is 3.29 per 100,000 population; more than twice the death rate from poliomyelitis.

2. A physician is bound to exercise such reasonable care and skill respecting the administration of the anesthesia as is usually exercised by the average physician and surgeon in the community. Before he is held liable for malpractice he must have done something which the recognized standard of medical practice in his community forbids or must have neglected to do something required by those standards.

3. A nurse anesthetist must administer anesthesia under the

supervision or direction of a licensed physician. If the nurse-anesthetist would act independently, this would constitute the practice of medicine. Where she follows the instructions of the physician she is protected by the element of control.

The legal question always is: did she breach the duty which the law imposes upon her?

Whenever acts are carried out by persons in the employ of the hospital but under the supervision and control of the physician, he thereby becomes responsible for their acts.

In all hospitals there is a need for the supervision and thorough training of all nurse-anesthetists.

4. When the doctrine of "res ipsa loquitur" ("the thing speaks for itself") is applied, a presumption of negligence on the part of the physician exists. He then must prove his own freedom from negligence.

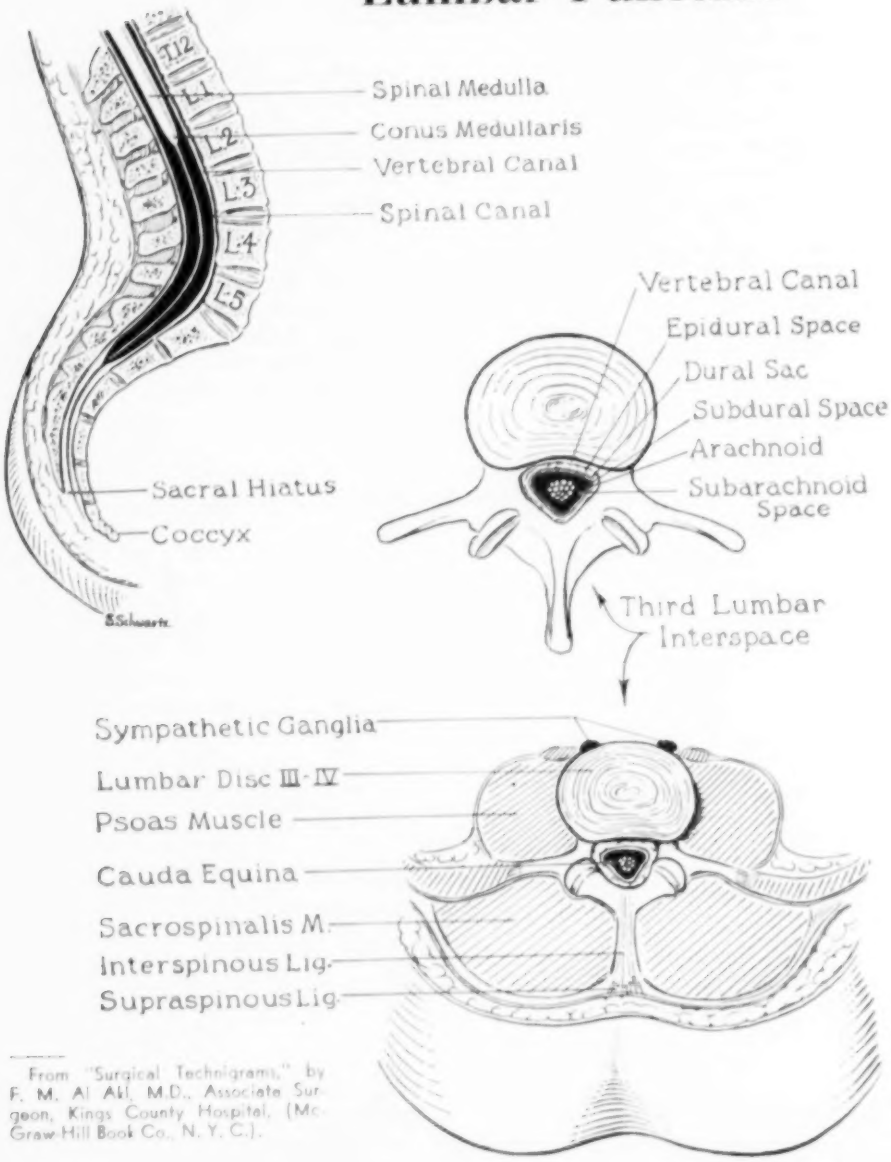
5. Proper pre-operative and pre-anesthetic examination and comprehensive laboratory tests must be carried out on all candidates for anesthesia. During the anesthesia due care must be exercised and any danger signal must be evaluated. All apparatus must be in working order with all possible sources of ignition eliminated.

Since static electricity is the most common cause of fires and explosions during anesthesia it must be eliminated in order to prevent accidents.

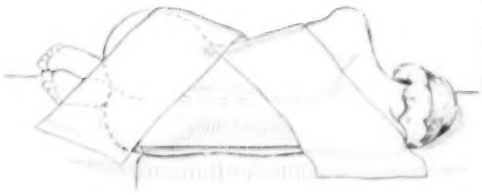
Bibliography

1. Ether Analgesia for Cardiac Surgery: Joseph Artusio Jr. M.D. and Frank Glenn M.D. An Audio Production Movie 1954
2. Study of Deaths Associated with Anesthesia and Surgery: Drs. Beecher and Todd; C. C. Thomas 1954
3. Static Electricity in Hospital Operating Suites: Bulletin 502 Bureau of Mines, U. S. Gov't Printing Office Washington 1953; Guest P. G., Sikora V.W., Lewis, Bernard.
3a. Philipp v. Shaw Prospect Heights Hospital, N. Y. App. Div. 2d Dept.—Nov. 24, 1952
4. Meyer vs. St. Paul Mercury Indem Co. of St. Paul Minn. 73 So. 2d 781
5. Nelson v. Murphy 258 P. 2d 472
6. Muehlenbeck v. Parke Davis Co. 141 Minn. 154, 169 N.W. 541 145 Minn. 100, 176 N.W. 169
7. Schloendorff v. New York Hospital 211 N.Y. 125, 129, 132
8. Barker v. Hanny 82 S.W. 2d [417] Texas
9. Woodson v. Huey 261 P. 2d 199
10. Some Legal Responsibilities of Nurses: Plant, M. L. Hospitals Sept. '53 P. 94
11. Kamalyan v. Henderson 277 P. 2d 372
12. 41 Am. Jur. Physicians and Surgeons Sec. 95
13. Jackson Admr. v. Joyner N.C. Sup. Ct. Oct. 2, 1952
14. Wintenton v. Semler 255 P. 2d 138
15. Ardolino v. Keegan 102 A. 2d 352; 140 Conn. 552
15a. Anesthesia and Allergy: Adrian J. Ann. Allergy 12: 549-554 [Sept.-Oct. 1954] St. Paul
16. Bernsden v. Johnson 255 P. 2d 1033
17. Porter v. Puryear 258 S.W. 2d 182
18. Piss v. 83rd Foundation 69 N.Y.S. 2d 727
19. 38 Am. Jur. Neg. #295 P. 989-991
20. Kichen v. Fein 104 Ind. App. 606
21. Lincoln et al. v. French 105 U.S. 614,617.
22. Swartout v. Holt 272 S.W. 2d 756

Lumbar Puncture

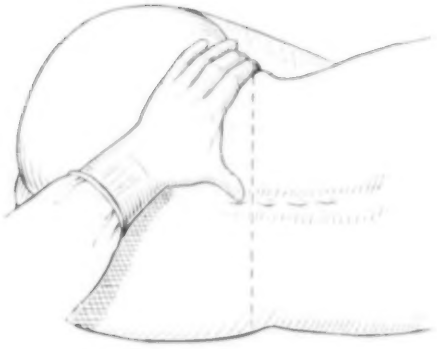


From "Surgical Technigrams," by F. M. Al Ali, M.D., Associate Surgeon, Kings County Hospital, (McGraw-Hill Book Co., N. Y. C.).



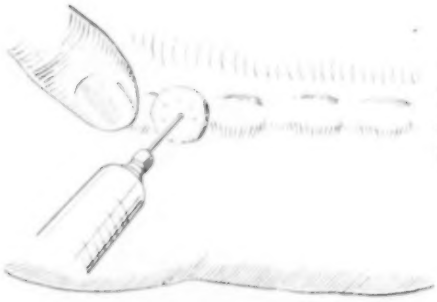
1

Place patient at edge of operation table. Arch spine by flexing knees and head. Maintain hips and shoulders in vertical plane. Paint and drape operative field.



2

Apply fingers to projecting iliac crest. Place thumb over spine at intercrestal line. This line crosses spine at fourth lumbar interspace.

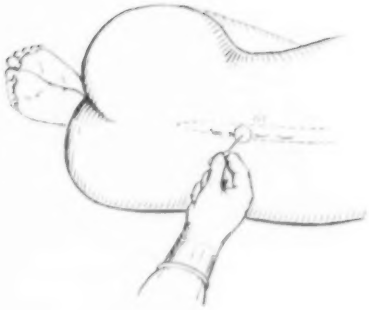


3

Move thumb to proximal (third) interspace. Raise intradermal anesthetic wheal between delimiting spinous processes.

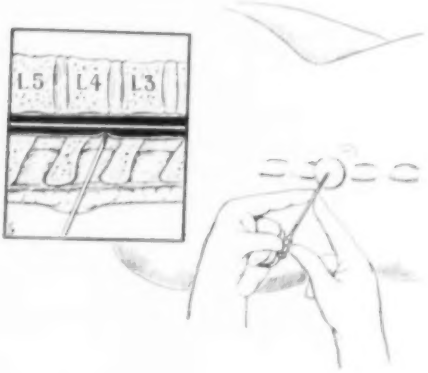
4

Introduce spinal needle into interspace at superior border of fourth caudal spinous process. With a firm grip, advance needle forward and slightly upward in direction of umbilicus.



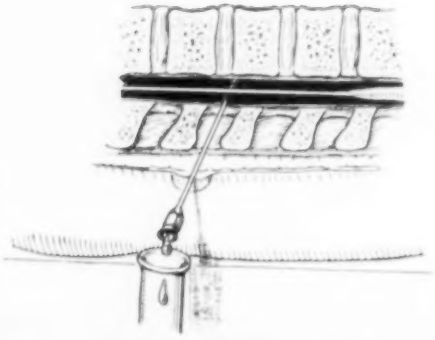
5

Advance needle further until sudden diminution of resistance announces entrance of needle into spinal canal.



6

Push needle to anterior wall of spinal canal. Withdraw needle one or two millimeters. Remove stylet. Collect fluid.



LUMBAR PUNCTURE NOTES

Anatomy The *vertebral canal* comprises the series of vertebral foramina which extend from the foramen magnum at the base of the skull down to the tip of the sacrum. The canal is lined by a fibroendothelial sheath composed of the dura mater on the outside and the arachnoid on the inside. The dura mater is a fibrous sheath and is separated from the bony canal by adipoareolar tissue. The arachnoid is a delicate endothelial membrane which encloses the spinal fluid-filled subarachnoid space. Within this fluid bed the spinal cord, dressed in its intimate tunic of pia mater, lies suspended and anchored to the spinal parietes by the spinal nerves.

In the embryo the *spinal cord* fills practically the entire spinal canal. With age the bony vertebral column grows faster than the spinal cord. As a result the cord rises by its more fixed cephalic extremity. At birth the tip of the cord (conus medullaris) commonly rises up to the fifth lumbar vertebra. In the adult the conus medullaris may lie at the first lumbar interspace or as high as the body of the twelfth thoracic vertebra. From that height, like the tail of a horse (cauda equina), the sacral and coccygeal nerves run vertically caudad toward the sacral and coccygeal foramina.

Technique The arachnoid lining of the vertebral canal grows with the vertebral column, and the subarachnoid space continues to extend halfway down the sacral hiatus. The slower-growing spinal cord rises, meanwhile, almost up to the thoracic segment of the spine. This interval between the conus medullaris above and the end of the subarachnoid space below is utilized for lumbar puncture.

The subarachnoid space contains about 175 cc. of cerebrospinal fluid. The fluid is maintained under varying degrees of pressure. This pressure and the bore of the needle employed determine its rate of flow during spinal tap.

In the infant the distance between the skin surface and the vertebral canal at the third lumbar interspace is approximately 2 cm. It increases with age and is usually 6 to 7 cm. in the adult, depending on the amount of subcutaneous fat present. The distance may be as much as 12 to 15 cm. in an obese person.

The spinal-tap needle may be introduced either in the midline between the spinous processes of the lumbar vertebrae or posterolaterally between the vertebral laminae. The tap may be effected with the patient sitting up or lying on his side at the edge of the operation table. Besides the added comfort to the patient, the recumbent position permits the operator to place a sterile towel over the iliac crest. The crest remains available for ready palpation and selection of the desired interspace. This obviates the necessity of "digging" into the lumbar skin with the fingernail to mark the commonly utilized third interspace.

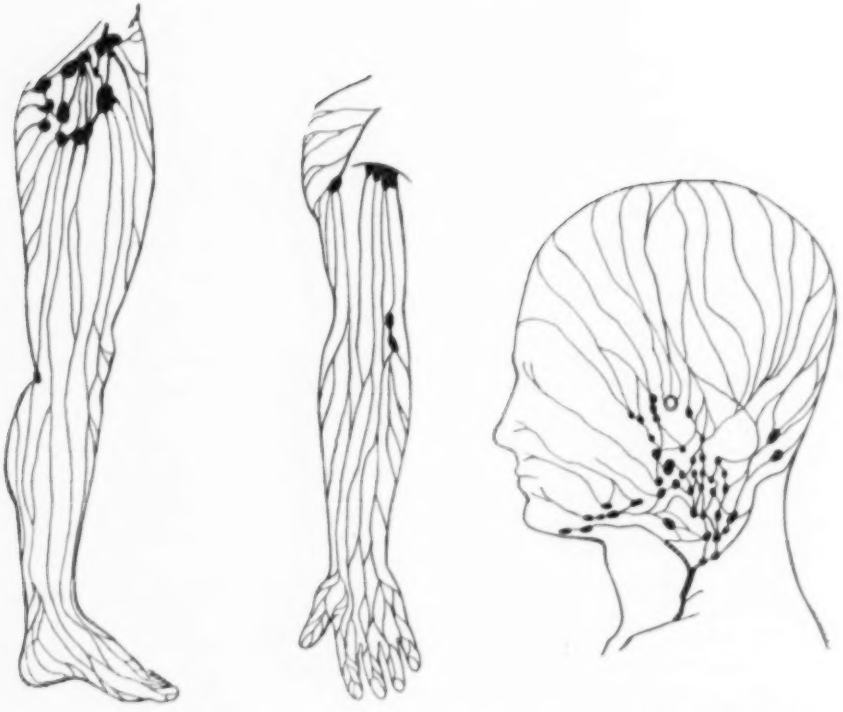
The structure and position of the vertebrae vary, and with them the direction of the interspinous spaces. Flexion of the spinal column fans out the spinous processes and opens the spinous interspaces. This facilitates the introduction of the needle into the spinal canal. If the needle meets with resistance it is withdrawn slightly. The spine is further flexed, and the needle is advanced again; or the needle is withdrawn and the cephalic interspace is tried.

With experience it becomes easy to

feel the sudden diminution of resistance as the needle pierces the tough dural covering and enters the intrathecal space.

Until sufficiently experienced, one may be guided by reaching the resistant anterior wall of the vertebral canal, then slightly withdrawing the needle into the subarachnoid space before removing the stylet for the tap.

Clini-Clipping



Lymph vessels and lymph nodes of the most common sites of lymphangitis. Note that the ulnar side of the palmar aspect of the arm drains into the cubital nodes and the lateral side of the foot drains into the popliteal nodes.

Clinico-Pathological Conferences

New York University-Bellevue Medical Center Post Graduate Medical School, Department Of Medicine at Bellevue Hospital, Fourth Medical (N. Y. U.) Division

PATIENT M. D.

A 63-year-old married Russian male was admitted to the Dermatology Service of Bellevue Hospital on 12/16/53 because of blue "spots" on his legs. The patient had been in good health until 5 months prior to this admission when he first noticed a few red blotches of the legs and swelling of the ankles. He became anorexic and lost 13 lbs. He developed pallor, weakness, night sweats; and cough productive of bloody sputum on several occasions.

The above picture progressed and the patient reported to the 4th Medical O.P.D. where positive physical findings included several purpuric spots on the hard palate and a purpuric eruption over both lower legs, and emphysematous chest, BP 120/30, swelling and tenderness of both ankles, clubbing of the fingers and toe nails. No heart murmurs were heard and a Rumpel-Leede test was negative. A CBS at that time revealed: RBC: 4.07, WBC: 6750, Hgb. 11.5 gm., Polys 43, Trans. 1, Lymphs 49, Mono 2, Eos. 1. The lymphocytes were "small and mature". Platelets: 133,000. Clotting time: 7½ minutes, bleeding time: 1 minute. Chest film revealed para-hilar fibrosis, accentuated bronchovascular markings, and a calcific density in the right base.

On admission to Dermatology a medical consultation was requested and the physical findings were unchanged except for the notation of a harsh Grade II systolic murmur heard best at the aortic area, radiating up the neck vessels and down the left sternal border.

A urinalysis revealed: Sp.Gr.: 1015, Alb 1+, Sugar 0, WBC: 1-2, RBC 15-20.

The patient insisted on signing out of the hospital against advice on 12/18/53 and was therefore referred by the medical consultant (to the Hematology Clinic). When he was seen one week later in the Hematology Clinic, bilateral axillary adenopathy was noted. The CBC was essentially unchanged, platelets were adequate on smear, and one "plasmoid cell" was noted. The patient refused bone marrow aspiration and lymph node biopsy. In March, 1954, he was seen in the clinic; at this time he complained of abdominal pain and at the same time was noted again to have a lower leg purpuric eruption. The patient was treated with pyribenzamine.

Labortory Data

4/12/54	CBC.	Hgb.	6.5 gm.	RBC. 2.4	WBC 10,750	Trans	20
		Hct.	19%	ESR 76		Polys	56
		Retic	7.6%	Platelets 130,000		Lymphs	28
						Mono	6.
	Urine:	Sp. Gr.	1013	4 + alb.	10-12 WBC.	10 RBC.	
				Many hyaline and gran. casts.			
	CO_2	16 meq.		A/G 2.9/4.8	Creatinine	3.9	
	Na	136		K 6.8	Chol/Esters	176/84	

Three series of blood cultures: Negative on aerobic and anaerobic culture.

Sputum for AFB-negative on 5 occasions

Sputum smear:	Gram. pos. and neg. cocci
Sputum culture:	Occas. Strep. viridans.
Rumple-Leede—	Negative on 2 occasions.
Skin biopsy:	Atrophy of striated muscle, slight, with hemosiderin pigmentation.
Pt. Chest:	Irregular area of diminished illumination in right parahilar region. Widespread increase in pulmonary markings previously noted has subsided, except for right para-hilar area.
EKG's 4/11—	Sinus tachycardia, QRS transitional zone shifted to left. Initial T-wave depression of non-specific nature I, II, III, avf, V6. This type of EKG is often seen in pulmonary embolism.
4/29—	No significant change.

Because of a low grade fever, a 16 day course of terramycin was instituted. Blood cultures had not been done. He was also given Vitamin K, ascorbic acid, and ferrous sulfate. The patient received a blood transfusion and was digitalized with digoxin.

Further laboratory work-up revealed the following:—

4/20/54	Hgb. 10.5	RBC. 3.8	Hct. 36%				
	Platelets 58,000.						
	Urines: 4/15/54	Sp. Gr.	1007	Alb.	0	2-3 WBC.	20-25 RBC. several gran. casts.
	Urines: 4/24/54	Sp. Gr.	1009	Alb.		Sl. Trace	Loaded with Rare WBC. RBC. few RBC. casts.
	Urines: 4/30/54	Sp. Gr.	1010		30 mgm.	3-4 WBC.	30-40 RBC.
	Urines: 5/5/54	Sp. Gr.	1008		20 mgm.	5-7 WBC.	many RBC. few gran. casts.

Mazzini — positive.

On his second admission (4/11/54), the patient complained of chest pain which had its onset 3-4 days before, did not radiate, and was not related to position, eating, or respiration. He again complained of cough with hemoptysis.

The physical findings were as follows: Temp. 100°. PR 84/min. RR 20/min. BP 130/53. The patient appeared acutely and chronically ill with rather severe dyspnea. The fundi showed flame shaped hemorrhages adjoining each disk. There were 2 areas of ecchymosis on left buccal mucosa. The neck veins were distended and there was a positive hepatojugular reflux. There were coarse rales in both bases posteriorly. The heart: Point of maximum impulse not felt, high pitched musical systolic murmur heard best 5 cm to the left of ensiform process. P2>A2, RSR. The liver was enlarged 2 cm. below the costal margin. There were coalescent purpuric spots on both lower legs, 4+ pitting pretibial and ankle edema, and 3+ clubbing of the fingers. There was no glandular enlargement.

The patient received intermittent mercurials and about 1 week after cessation of the terramycin therapy, a series of blood cultures were taken and he was started on streptomycin and large doses of penicillin. Shortly before initiation of this therapy, a soft, blowing early diastolic murmur was heard at the base, along with the finding of a Durozier sign. The blood pressure was 140/50.

The penicillin injections were refused most of the time. After 19 days of this therapy, the regime was cut and terramycin, 500 mgm. Q 6 h. was restarted. The patient remained afebrile after the onset of penicillin and streptomycin therapy, as opposed to his earlier chronic low grade fever. Gradually, however, he became weak and moribund and died quietly on his 65th hospital day (6/4/54).

Laboratory data at the end of his course included the following:

Hgb. 8.5	RBC. 3.10
Platelets	19,000
Creatinine	2.7

Pathological Findings

The heart was slightly hypertrophic; it weighed 400 grams (the patient was only 5′ 4½″ tall). There was slight dilatation of the left ventricle, but the other chambers were of normal size. All the valves were normal, except the aortic. The aortic valve was bicuspid. Before it was opened, it appeared to be grossly incompetent. A large part of both valve cusps was replaced by large bacterial vegetations. In addition, a mycotic aneurysm had burrowed into the aortic wall in the left sinus of Valsalva. The only evidence of a possible raphe representing the missing third commissure was a small ridge on the aortic wall at the base of the sinus of Valsalva in the center of the larger of the two cusps; this cusp was just twice as large as the other one. There was abundant vegetation in the immediate vicinity of the ridge, and there were two small perforations in the adjacent cusp.

Histologically, there was abundant evidence of inflammation in the presumed abortive raphe as well as elsewhere in the valve. The presence of vegetation at this site makes it impossible to apply the usual criteria for differentiation between congenital and acquired bicuspid valves[1,2]. The *subacute bacterial endocarditis* may have been

superimposed on a congenitally *bicuspid aortic valve*, or bacterial endocarditis may have destroyed one of the commissures of a previously three-cuspid valve. Post-mortem culture of the blood was sterile. Enterococci were cultured from a vegetation, and cocci were seen in the sections of vegetation.

There was abundant evidence of embolic phenomena from the bacterial vegetations. There was mild focal myocarditis associated with minute organizing myocardial infarcts. A mycotic aneurysm was found in the superior mesenteric artery. The spleen contained two infarcts. The kidneys showed *focal embolic glomerulonephritis*, a not uncommon complication of subacute bacterial endocarditis. An interesting feature of this lesion was the fact that all of the glomerular damage from it was subacute or chronic. This suggests that some benefit was derived from the antibiotic therapy administered terminally. In addition, the kidneys showed mild *acute diffuse glomerulonephritis*. This disease has been reported in increased incidence in patients with bacterial endocarditis.[3]

The right upper lobe contained a large multiloculated abscess, surrounded by an area of organizing pneumonia. This abscess was probably not due to an infected embolus from the endocarditis, because the only route such an embolus could have taken would have been through a bronchial artery. More probably bacteremia, secondary to the endocarditis, or infected material from one of the metastatic lesions in heart, spleen or kidney traveled to the lung via the systemic venous system.

References

(1) Simon Koletsky: Acquired bicuspid aortic valves. Arch. Int. Med. 67, 157, 1941.

(2) L. F. Bishop, Jr. and M. Trubek: Bicuspid aortic valve: a differential study between inflammatory and congenital origin. J. Tech. Methods 15, 111, 1936.

(3) Herman Villarreal and Leon Sokoloff: The occurrence of renal insufficiency in subacute bacterial endocarditis. Am. J. Med. Sci. 220, 655, 1950.

PATIENT P. H.

A 64-year-old white male was admitted to Bellevue Hospital on 4/29/54 with hematemesis and epistaxis. Two weeks prior to admission the patient experienced dizziness, and several bouts of vomiting, followed by the passage of black stools. He developed progressive weakness and fatigue. For the two days prior to admission he had bleeding from the nose and vomited bloody material which he swallowed from the epistaxis.

The patient gave a six month history of pain in both sides of the back radiating to the lower quadrants, severe and intermittent, with bloody urine accompanying the pain. There was a history of renal disease known since 1943 with frequency and nocturia. He was also told that he had hypertension.

The admission laboratory work revealed the following:

Urinalysis: cloudy, 1010, 4+ albumen, loaded — RBC & WBC

Hgb.—11 gm. Hct 37 ESR—108

BUN—113. Mazzini—negative

Prothrombin Time—100%

CO_2—15 meq. Platelets 270,000

Stool Guaiac—4+ (on admission later became negative)

On physical examination the patient was found to have dried blood in the left nostril and throat. BP 170/108 PR-86 Temp.-99°. The fundi revealed some A-V nicking and "silver-wiring". There was no hepato-jugular reflux. The lungs revealed expiratory wheezes and rhonchi. The heart revealed: PMI VI ICS 2 cm outside the midclavicular line, no murmurs. There were no organs or masses palpated in the abdomen. There was a mottled cyanosis of the lower extremities.

On 4/30/54 the patient was given one pint of blood. Cystoscopy and retrograde pyelography performed on 5/9/54 revealed a severe cystitis and trigonitis, and slight hydronephrosis. Urine from

Date	Urine Sp. Gr.	Urine Alb.	Urine RBC	Urine WBC	Hgb.	ESR	Creat-inine	CO_2	Na	K	P	Ca	Chol. Ester.	A/G
4/29	1010	4+	loaded		11	108		15						
5/8	1010	4+	many											
5/10	1009	400 mg%	Cath. 1-2	5-7	10.5	65	11.4	20	131	3.08	9.6	5.7	440	
5/11	1009	500 mg%	Cath. many	5-8			11.4						270	
5/13							9.2	18			8.0	7.4	190	
5/17	1009	500 mg%					9.4	11	132	4.8	10.4	7.6		1.5 4.7 2.1
5/19	1009	600 mg%	3-4	2-4			10.2	10	133	5.2	9.1	8.2		5.1
5/20								10	127	5.4				
5/21					11.5	61	12.2	8	131	5.12	8.0	9.5		
5/24							11.1	15	142	4.26	9.1	7.0		
5/26							11.0	13.5	128	4.04	9.1	7.7		
5/28							12.4	13.5	140	4.2	12.0	7.0		
6/1							12.2	11	148	4.0				
6/3							12	13	136	3.8				1.5
6/7							12.2	9	135	3.9	7.2	5.2		2.4

both right and left ureters showed many WBC & RBC. Cultures revealed: Rt ureter — B. coli Left Ureter — B. proteus.

The patient was given intravenous fluids (glucose/water, normal saline, 1/6 Molar Lactate, Gantrisin and terramycin. On 5/12 the diet was changed to low protein. The potassium and phosphates continued to climb and the CO_2

decreased. Sodium bicarbonate was given and Thorazine was then added to the therapy in an attempt to reduce the emesis. Amphojel was given to bind the phosphates. A Foley catheter was inserted to relieve any obstruction that might exist.

On 5/20 generalized twitchings were noted for which the patient was given intravenous calcium gluconate. Plasma was given because of the low serum albumen. A renal biopsy was performed on 5/21.

The patient continued to do poorly and on 6/9/54 quietly expired. He was afebrile during entire hospital course.

Summary of the laboratory data can be found on page 941.

Pathological Findings

The kidney biopsy, taken on 5/21/54, showed *renal amyloidosis* (Surgical #2859-54). The minute fragment of tissue available afforded no further information.

Autopsy was performed five days after death. The kidneys were small (110 and 120 grams, respectively). Histologically virtually every glomerulus was replaced by amyloid. There were also amyloid deposits in the basement membranes of some collecting tubules. In addition to the amyloidosis, the kidneys were extensively scarred and contained large aggregates of chronic and some acute inflammatory cells. No obstruction or other explanation for the *acute* and *chronic pyelonephritis* was found. However, the patient also had *acute prostatitis*.

There was extensive *amyloidosis* of the *adrenals*, and arterioles in several organs were markedly thickened by deposits of amyloid. No amyloid was found in liver or spleen.

An acute and an early chronic ulcer were found in the duodenum. We have no explanation for these lesions. There was also acute colitis and proctitis, a common finding in uremia. The positive stool guaiac might have been due to either the duodenal or the colonic lesions, or to swallowed blood following the patient's epistasis.

The patient's heart was hypertrophied (600 grams), probably as a result of his hypertension. His lungs showed chronic passive congestion and *lobular pneumonia*. An incidental finding was *syphilitic aortitis*.

The pattern of distribution, with involvement of kidneys and adrenals, was compatible with the diagnosis of "secondary" amyloidosis. Chronic pyelonephritis has been reported as a cause of amyloidosis, but with insufficient frequency to make the association more than speculative. The involvement of arterioles is not characteristic either of primary or of secondary amyloidosis. Arteriolar amyloidosis was an atypical characteristic of another recent autopsy (40772, CPC of October 28, 1954). Renal amyloidosis is not generally associated with hypertension. Chronic pyelonephritis sometimes is.

Cases presented from the wards of the Fourth Medical Division, Bellevue Hospital, Dr. Charles Wilkinson, Dir.

Treatment of Hemangiomas

Hemangiomas are the most frequently encountered skin lesions of infancy and childhood which require proper evaluation and treatment. Although it is true that some may involute spontaneously others on the other hand may grow and cause destruction. It is therefore important to learn to differentiate these lesions so that proper therapy can be instituted early when it is most effective.

In addition to these congenital hemangiomas, other types of acquired hemangiomas should be recognized. Certain of these are important because they represent external manifestations of internal diseases, others because they must be differentiated from malignant lesions.

Nevus Flammeus (Port Wine Mark) This is a flat lesion of various size and of varying depths of red. It appears as a deep red staining, the skin being otherwise normal. The common sites are the face, neck and upper parts of the thorax. This type persists throughout adulthood. Rarely, it is associated with calcifications in the brain of the same side as the lesion, with paresis or paralysis of the opposite side of the body (Sturge-Weber syndrome).

A flat type of hemangioma, localized to the nose or the neck, is found in ⅓rd of babies at birth. It often disappears spontaneously but may persist into adulthood.

A related type consists of ill-defined pinkish red staining found in babies at birth and symmetrically distributed over the eyelids, the glabella and the mid-

Fig. 1. Nevus flammeus—Flat dark red discoloration of the skin, commonly seen on the face and unilateral.

Fig. 2. Strawberry Mark—Sharply circumscribed and elevated vivid red lesion—It has a mammilated surface and is compressible.

portion of the face. Its only importance is to differentiate it from the unilateral persistent nevus flammeus. It always disappears and within a short time; parents may therefore be reassured accordingly.

The treatment of nevus flammeus is on the whole unsatisfactory. It does not respond to radium or roentgen ray therapy. In recent years, the application of solutions of thorium X has produced satisfactory results in some cases. Tattooing the lesion with skin colored pigment is a long tedious procedure which again has produced satisfactory results in some cases. It is more effective when the capillary plexus is situated deep enough to allow the interposition of pigment between it and the epidermis. In adult women, the lesion may frequently be adequately camouflaged by the application of certain cosmetics which are now available for this purpose.

Superficial Angiomas (Strawberry Mark) This lesion is circumscribed, elevated, strawberry to raspberry colored, and finely lobulated. It is compressible and blanches on pressure. It may occur anywhere on the body.

This lesion will in most instances involute spontaneously within a few years. When it is on the exposed portions of the body, the parents may nevertheless be anxious to have it treated. Refrigeration with solid carbon dioxide produces excellent results; only a few treatments are usually required. Beta rays of radium and grenz rays are also used successfully.

Cavernous Angiomas These constitute the most common type of hemangiomas. They consist of irregularly shaped boggy-masses which are situated in the corium and are compressible. The overlying skin is usually flat or slightly raised and has a blueish discoloration. This lesion is palpated rather than seen.

It may be present alone or with a superimposed strawberry mark. Therefore when one is presented with a strawberry mark, it is most important to palpate it to determine the presence or absence of a deep cavernous element.

The cavernous angioma may undergo spontaneous involution but frequently persists and increases in size. Many dermatologists elect to treat them as soon as they are detected since they are most responsive to treatment in the early stages. One may also be ultraconservative and observe it for a few months; if it tends to increase in size, treatment should be promptly instituted.

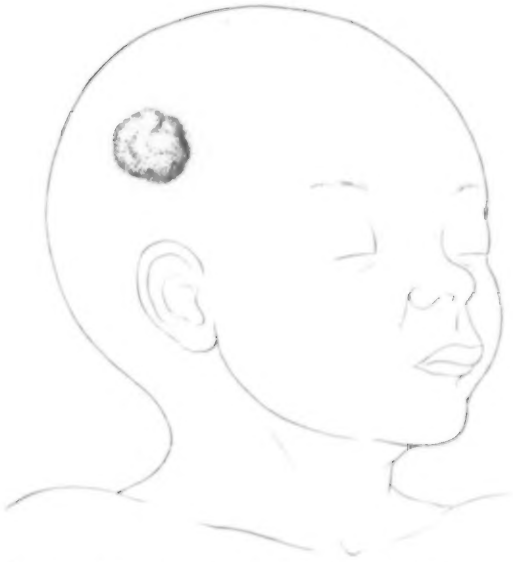


Fig. 3. Cavernous Angioma—Deep boggy mass causing a slight elevation and bluish discoloration of the skin—A strawberry mark often overlies this lesion.

These lesions are very responsive to small doses of radium or superficial roentgen rays. Sclerosing solutions are used much less now. It is a painful procedure and the danger of sensitization is ever present. In addition, some of the lesions situated about the head and neck may communicate through a venous channel with vital internal structures.

Occasionally, following the involution of the cavernous mass with radiation, excess loose skin may remain. If this defect does not correct itself with the growth of the child, it can be removed by plastic surgery.

Nevus Araneus (Spider Nevus) This lesion consists of a slightly raised pinhead size punctum from which several dilated capillaries radiate like legs of a spider. When the central portion is compressed with the head of a straight pin, the entire lesion blanches; this differentiates it from a petechia. These lesions are found most commonly on the dorsa of the hands, face and chest.

When several lesions are present in childhood, an hereditary cause is often suggested. This is the case in Osler-Weber-Rendu Syndrome, in which multiple lesions may be found not only on the skin but on the lips, buccal mucosa, tongue, and mucous membrane of the nose and entire gastrointestinal tract, giving rise to epistaxis and gastrointestinal hemorrhages.

Spider nevi may also be found associated with hepatic diseases, scleroderma and pregnancy.

There is a pulsating type of spider nevus arising about the eyes and on the dorsa of the hands which is found in association with hepatic diseases, especially cirrhosis of the liver.

Spider nevi are best treated by applying the needle of the desiccating machine to the center of the lesion.

Senile Angiomas These are small pinhead to split pea sized, ruby colored, elevated rounded lesions which do not blanch on pressure. They are seen on the torso of adults. Their only importance lies in the fact that they should be recognized as such: a harmless lesion of no clinical significance.

Angiokeratomas These are dark red elevated rounded firm lesions having a keratotic surface. They are found on the scrotum, associated with varicosities

of that location, or on the labia-majora. They may sometimes rupture and bleed, causing undue alarm.

These lesions may be easily treated with the surgical diathermy unit.

A similar more keratotic variety is found on the dorsa of the hands, knees and feet. These latter are frequently on an hereditary basis. When single they may be confused with melanomas. The finding of other similar lesions on the above mentioned locations easily rules out that possibility.

Summary

The three main types of congenital angiomas are discussed. Tattooing of skin colored pigment or the use of solution of thorium X offer some promise in the treatment of the nevus flammeus, a heretofore hopeless condition. Strawberry nevi almost always disappear spontaneously, but their involution may be safely accelerated by the application of solid carbon dioxide or the beta rays of radium. Cavernous hemangiomas may disappear spontaneously but frequently increase in size and cause destruction; they are best treated early in infancy or at least when any sign of growth is observed. The gamma radiation of radium or superficial roentgen rays give excellent result.

The importance of acquired angiomas such as spider nevi, senile ectasias etc., lies mainly in recognizing them as benign entities and in bringing attention to some underlying disease, such as cirrhosis of the liver.

STOP!

at "Coroner's Corner"
Page 29a

Read the stories Doctors write of their unusual experiences as coroners and medical examiners.

—in every month's issue of

MEDICAL TIMES

EDITORIALS

H. Sheridan Baketel, A.M., M.D., F.A.C.P

The late Doctor Baketel's editorial career encompassed *Gaillard's Medical Journal*, the MEDICAL TIMES, and *Medical Economics*, the last founded by him in 1923, which symbolized a new era in medicine, taking account for the first time, and constructively, of a new phase of practice quite as important as any other professional activities, and vesting it with dignity and many other significant values.

After country practice in New Hampshire, following his graduation from Dartmouth, Doctor Baketel began to practice in New York City in 1910. From 1915 to 1931 Doctor Baketel was Professor of Preventive Medicine at Long Island College of Medicine. He directed the physiological laboratories of Reed and Carnrick (from 1925), was chairman of the trustees of the Columbia University College of Pharmacy (1933-1942), and was president of the American Pharmaceutical Manufacturing Association (1929-1931).

As teacher, practitioner, editor, executive and soldier, Doctor Baketel's engaging human qualities always engendered the highest esteem.

Cult Versus Orthodoxy

According to the findings of the A.M.A.'s Cline Committee, reported at the Atlantic City convention in June, 1955, the deans and faculty members of the schools of osteopathy are doing their best to teach the scientifically recognized principles of medicine, with little concern about cultist concepts.

The A.M.A.'s reference committee at the Atlantic City meeting recommended (5 to 1) that doctors of medicine be permitted to teach in schools of osteopathy without the stigma of ethical violation.

The idea seems to have been to raise the osteopathic teaching level and to bring the osteopaths into the future fold of established medical practice.

The dissenting member of the reference committee (M. O. Rouse of Texas) argued that the osteopaths should go to

medical schools and become doctors of medicine.

If osteopaths are able to pass the New York State Board of Medical Examiners, and are licensed to perform any medical or surgical service just like regular physicians, one wonders why such men did not study medicine and qualify in a conventional way. They must have the same capacities and qualifications.

"Metaphysical" Medicine

An article in *Psychosomatic Medicine* (16-478 Nov., Dec., 1954) by four authors of note makes a comparison of blood pressure response to Veriloid and *to the doctor himself*. It undertakes to show that the effects of antihypertensive drugs are determined in part by the psychological attitude of the examining clinician. The authors actually found that the enthusiasm and therapeutic sincerity of the clinicians accounted for lower pressures; higher pressures were noted when the clinicians were skeptical and without interest; the difference could not be ascribed to the drug itself.

An obvious fallacy here can easily be pointed out. How can skepticism and lack of interest be self-induced by the examiner when not justified by a given clinical situation?

We don't doubt for a moment that the blood pressure findings were as recorded but we think that other than "metaphysical" factors must have been involved.

Congressional Casualties

Newspaper correspondents in Washington are increasingly perturbed by the mounting Congressional casualty lists. Beginning with Senator Johnson of Texas a long line of our statesmen have gone down like ninepins with all sorts of breakdowns. The gentlemen of the press are not surprised at the morbidity and mortality, for they have been first-hand witnesses of how our legislators, under pressure, squander their vitality. The strain is too much for men who as a rule are not paragons of physical integrity.

"The leaders of Congress are overburdened and reorganization of their duties should be arranged to lighten them" (*New York Times* July 7, 1955).

"MEDICAL TEASERS"

A challenging crossword puzzle for the physician

page 41a

MEDICINE

MALFORD W. THEWLIS, M.D.*

The Home Management of Tuberculosis With Newer Drug Therapy

D. R. McKay (*New York State Journal of Medicine*, 55:87, Jan. 1, 1955) reports that in Erie County, New York, there are two clinics to aid in the treatment of patients with tuberculosis; one of these clinics is under the direction of the Erie County Department of Health and the Buffalo and Erie County Tuberculosis Association, and the other is at the Erie County Hospital. The care of patients in these clinics is not designed to interfere with medical care by private physicians, but to supplement it. Only certain types of cases are selected for home treatment. In the first place the patient must be "a reported case" of tuberculosis with clinical and laboratory evidence to substantiate the diagnosis. Before home treatment the patient should usually have a minimum of six months of hospital or sanatorium care. The home environment must be suitable, in regard to space, provision of care, opportunities for recreation. Protection of other members of the household, particularly children, is essential. The patient should have the type of tuberculosis that can be benefited by the modern anti-tuberculosis drugs. At the County Hospital Clinic, a few patients have been admitted who had not been hospitalized, but were found to need drug therapy. No evaluation of the clinical benefits derived from the home care of the patient with the aid of the clinics can be reported at present until the plan has been in operation for one year, but it is evident that the clinics maintain more adequate supervision of the patient and his family with the cooperation of the family physician and provide more adequate drug treatment. A large percentage of the patients registered at the two Erie County clinics are over forty years of age, an age group that often finds it "difficult to adjust to a long period of hospital supervision" and can thus be especially benefited by adequately supervised home treatment.

Thewlis

Topical Isoniazid-Streptomycin Aerosol in the Treatment of Pulmonary Tuberculosis

E. J. Grace (*Antibiotic Medicine*, 1:23, Jan. 1955) reports the treatment

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of pulmonary tuberculosis by "multiple chemotherapy" including streptomycin and isoniazid (Streptohydrazid) aerosol, streptomycin and isoniazid given by injection, and para-aminosalicylic acid (PAS) and isoniazid given by mouth. The aerosol was given by the nasal route and the patient was instructed in inhaling deeply and forced exhalation so that aerosol mist would reach the periphery of the lung; the topical application to the primary focus of infection in the lung by means of the aerosol containing the combined agents (streptomycin and isoniazid) in a detergent solution, is an important factor in the treatment. The aerosol, combined with parenteral and oral therapy, was continued until cultures of gastric smears were negative and x-ray study of the chest showed healed lesions without cavity formation. A one-year follow-up of cases treated showed the improvement to be maintained and cultures remaining negative. While the follow-up period of one year is "rather limited," the author is of the opinion that the results indicate that the topical multiple chemotherapy can destroy the tubercle bacillus without the development of resistant strains. The author is of the opinion that the role of "bacterial genetics" is of importance in chemotherapy of infectious diseases, and that recent advances in the basic sciences should be more closely correlated with the use of chemotherapy not only in the treatment of tuberculosis, but in the treatment of other infectious diseases, as well, to prevent "the emergence of resistant bacterial strains."

COMMENT

This treatment should be further studied, especially in conjunction with the home treatment after the patient leaves the sanatorium.
M.W.T.

A Comparative Clinical Study of Several Enemas

S. G. Page, Jr. and associates (*Journal of the American Medical Association*, 157:1208, April 2, 1955) report a study of four enemas used in the treatment of 10 men, twenty-two to thirty-six years of age, who had chronic constipation. The four enemas studied were: the Fleet enema disposable unit, sodium chloride solution, soap suds enema, and tap water. In the Fleet enema solution, each 100 cc. contains 16 gm. of sodium biphosphate and 6 gm. of sodium phosphate; it is used in a 4.5 oz. plastic container that is disposable. The sodium chloride solution used as an enema was made with two teaspoonfuls of sodium chloride in one quart of tap water; the soap suds enema was prepared in the usual manner. The Fleet enema solution was given by squeezing the contents from the container, which was compressible; the other enemas were given with the usual type of apparatus. The preparation and administration of the Fleet enema solution required less time than any of the other enemas, averaging ten minutes and forty-five seconds, as compared with tap water, averaging eighteen minutes and thirty-four seconds, soap suds, averaging twenty-four minutes and fifty-eight seconds and sodium chloride solution, averaging thirty-eight minutes and thirty-three seconds. Sigmoidoscopic examination after the enema showed the sigmoid to be completely free of feces in 7 out of 10 cases after the Fleet enema, the other 3 showing "a few flecks" of feces or a small amount of fluid. After the plain water enema, the sigmoid was completely free of feces in only 3 cases, after the soap suds enema in only 4 cases, and after

sodium chloride enemas in only one case. Spasm or hyperemia did not occur after the Fleet enema; spasm occurred in one case after the soap suds enema, and in 2 cases after the sodium chloride enema; hyperemia was observed in one case after a plain water enema.

COMMENT

An interesting study which should be of value in everyday practice. There are times when adult size glycerin suppositories and ice bag ointment work satisfactorily in cases of constipation. M.W.T.

What the General Physician Should Know About Aviation Medicine

M. M. Kafka (*Journal of Aviation Medicine*, 25:639, Dec. 1954) states that the general physician must become familiar with the problems of aviation medicine, not only because he must often advise his patients as to desirability of travel by plane under certain conditions, but also because any licensed physician at present has the authority to make physical examinations for student and private pilots. In the examination of pilots, tests of vision and hearing are important, combined with the knowledge of the effect of different altitudes on these functions. A careful history and physical examination are necessary, a history of allergy, head injury or peptic ulcer is especially important, the condition of the heart and the blood pressure, the presence of obesity, and the effects of aging deserve special consideration in the selection of pilots; diabetes mellitus is a cause for rejection. Any pathological condition in the ear, nose, and throat should be carefully studied, especially because of the effect of altitude on such conditions. Antibiotics should not be used "indiscriminately" for infections of the upper respiratory tract, as antibiotics slow down the pilot's alertness. Pilot errors are still an important factor in aircraft accidents and the selection as well as the training of pilots is of importance in preventing such accidents. The author is of the opinion that it will be necessary either to discontinue "non-designated examiners" for selection of pilots or to have special courses in aviation medicine arranged for general practitioners through medical societies.

COMMENT

A field of growing importance since there is more and more travel by plane. M.W.T.

Oral Mercurial Diuretics: Mercumatilin in the Treatment of Congestive Heart Failure

S. P. Dimitroff and associates (*American Heart Journal*, 49:407, March 1955) report the use of mercumatilin (Cumertilin) given by mouth in the treatment of 25 patients with chronic congestive heart failure. Most of these patients were fifty to seventy years of age; 16 had hypertension either with or without arteriosclerosis, 3 had syphilitic heart disease and 6 had rheumatic heart disease. In all but 3 of these patients, symptoms were satisfactorily controlled by mercumatilin given by mouth. In most cases three tablets of mercumatilin three times a day, two or three times a week (an average of about one tablet daily) gave satisfactory results. The 22 patients who showed a satisfactory response to oral mercumatilin were able to maintain "their edema-free weight"; they showed no increase in liver weight, and no pulmonary rales. They showed less dyspnea and were able to carry on such activities as were allowed with less distress, and sometimes could increase

such activities without discomfort; their salt intake could be increased without ill effect. The 3 patients who failed to improve showed "unstable or rapidly progressive congestive failure." One of these 3 patients had gastritis and mercumatilin may have aggravated the gastrointestinal symptoms in this case. But otherwise there were no signs of toxicity or of intolerance to the drug in any of the patients treated.

COMMENT

An interesting study which should be continued. It would simplify the treatment if it could be done orally rather than by injections as this article suggests. M.W.T.

Treatment of Arteriosclerosis and Vague Abdominal Distress with Niacinamide Hydroiodide (Without Side Effects)

T. M. Feinblatt and associates (*American Journal of Digestive Diseases*, 22:5, Jan. 1955) report the treatment of 59 cases of arteriosclerosis with Niacinamide Hydroiodide combined with iodides. The medication was usually given by mouth, as tablets containing 135 mg. sodium iodide and 25 mg. Niacinamide Hydroiodide; at least two tablets a day were given. In some cases treatment was begun by intravenous administration of Niacinamide Hydroiodide (100 mg.) and sodium iodide (1 gm.) in 5 cc. twice a week; after one or two months, the injections were discontinued and the tablets were given. Of the 59 patients treated, the average blood pressure was 149/87; the blood pressure was not affected by the treatment; the group of patients included a few individuals who were overweight; the average weight was "within normal limits." There were 26 patients with arcus senilis, 36 with various degrees of enlargement, sclerosis and calcification of the aortic arch, and 18 with rubra; none of these conditions were affected by treatment. Forty-five patients showed vague abdominal distress, often associated with arteriosclerosis; the symptoms include nausea, flatulence, diarrhea, belching, constipation, epigastric pain, and spasticity; such symptoms were completely relieved by the treatment in 30 of the 45 cases, and partly relieved in 9 cases. Dizziness was a symptom in 55 patients; this cleared up completely in 39 cases after treatment; chronic headache was a symptom in 33 cases, and was completely relieved by treatment in 20 cases. Disturbed orientation, a symptom in 24 cases, was relieved in 12 of these cases; excessive fatigue, a symptom in 51 cases, was relieved in 21 cases. Improvement has persisted for more than a year while medication has been continued, but no signs of iodism developed, and there were no other ill effects of continued medication observed.

COMMENT

This requires a further study. It is difficult to say how many symptoms are due to arteriosclerosis and how many are not. It is rather difficult to determine to what extent arteriosclerosis is the cause of discomfort. There is no doubt that there are many symptoms of abdominal distress due to arteriosclerosis of the abdominal aorta which is seen by x-ray. It is in these cases that the effects of treatment can be judged. M.W.T.

SURGERY

BERNARD J. FICARRA, M.D.*

The Age Factor in the Mortality Rate of Patients Undergoing Surgery of the Biliary Tract

Frank Glenn and D. M. Hays (*Surgery, Gynecology and Obstetrics*, 100: 11, Jan. 1955) present a study of the mortality rate of 4,050 patients on whom biliary tract surgery was done. They note that the percentage of patients over fifty years of age who were operated on for biliary tract disease has shown a definite increase, for in 1933 of 176 patients operated on for non-malignant disease of the biliary tract, only 42 were over fifty years old, while in 1952 of 181 such patients, 106 were over the age of fifty. In the entire series of 4,050 patients, there was 1,355 who were fifty to sixty-four years of age, and 328 who were sixty-five years of age or over. The mortality rate due to postoperative complications was 2.5 per cent in patients fifty to sixty-four years of age and 6.7 per cent in the patients sixty-five years of age and over, as compared with 0.65 per cent in the group of patients under fifty years of age. In the group of aged patients (sixty-five years old and over), the mortality in elective surgical procedures was not significantly higher than in the younger age groups. For such elective surgery, the patients entered the hospital for a complete study of their biliary tract disease and also of other conditions present, and were adequately prepared for operation. It was in the emergency cases that the mortality rate in the aged group was much higher than in the younger patients. A study of these emergency cases in the aged group of patients shows an increased incidence of acute cholecystitis, as also noted by others "in every large series of geriatric biliary cases"; a relatively high incidence of choledocholithias with large and numerous calculi; minimal signs and symptoms of the acute process, increased incidence of neoplasia associated with non-malignant biliary tract lesions. The most frequent cause of death in the patients sixty-five years of age and over was, as in the younger age groups, hepatic insufficiency resulting from cirrhosis and infection; the second principal cause of death in this aged group was acute coronary occlusion. From this study, the authors conclude that surgery should be done for acute cholecystitis in older patients, but with "the most meticulous care in surgical management," including as early operation as possible before complications develop.

Ficarra

COMMENT

This study indicates that the patient of advancing years can and does fall victim to those

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diseases of the biliary tract usually associated with individuals in the forty year age group. This is an indirect compliment to modern medicine and surgery which is instrumental in prolonging human life so that today we see many elderly people pursuing daily activities on an equal plane with the youth of the nation. This survey indicates that the patient of advancing years with gallbladder disease and similar pathology can be treated like the patient of younger years. Surgeons can expect the same type of complications as with younger patients and they can feel safe in knowing that age is no longer a contraindication to necessary surgery. B.J.F.

Recurrent or Persistent Peptic Ulceration Following Secondary Operations for Peptic Ulcer

T. J. Everson and M. J. Allen (*American Surgeon*, 21:130, Feb. 1955) report that in a series of 90 patients with gastrojejunal ulceration, treated surgically 1946 to 1954, there were 11 patients who had recurrent or persistent ulcer symptoms and required secondary operations. Thirty-eight operations were done in these 11 cases; the number of operations for each patient varied from two to five (in 2 patients). Four operations were also done to close an ulcer perforation. A review of the cases showed, however, that only 24 of the 38 operations were operative procedures that are generally considered to be effective in the treatment of "the ulcer diathesis,"—either gastric resection or vagotomy. In this series of cases, vagotomy was done nine times, but the postoperative insulin test showed that the operation was completed in only 2 cases; in both of these cases relief from the ulcer symptoms resulted. Gastric resection was done 15 times, but 75 per cent or more of the stomach was resected in only 7 patients; relief of the ulcer symptoms resulted in 5 of these 7 patients; one patient died after operation; and one patient had a recurrence of symptoms, which were finally relieved by complete transthoracic vagotomy. Thus of the 11 patients studied, 2 were finally relieved of symptoms by complete vagotomy, and 5 were relieved following "adequate" subtotal gastrectomy. Two patients died, one after the gastrectomy operation (as noted above) and another died after four secondary operations following a gastric resection with less than 75 per cent resection. Two patients still have ulcer symptoms and "have refused further surgery." From this study the authors conclude that: Persistence or recurrence of ulcer symptoms after gastric resection or vagotomy is due "in most instances" to the fact that the operation is inadequate or incomplete. If ulcer symptoms occur after an adequate gastric resection (i. e., 75 per cent or more of the stomach resected), they can usually be controlled by complete vagotomy.

COMMENT

Every surgeon who has operated upon a reasonable number of patients with ulcers, has one or more of these patients who will need additional surgery for recurrences. No matter what procedure is performed and no matter who the surgeon may be recurrences are always with us. This series corroborates the finding that even multiple operations will fail to correct the underlying cause in certain individuals. B.J.F.

Clinical Observations on the Use of Alphaprodine (Nisentil) for Postoperative Analgesia

E. H. Bachrach and associates (*Surgery*, 37:440, March 1955) report a study of the value of Nisentil, a synthetic piperidine derivative, for postoperative analgesia, as compared with meperidine. There were 478 patients in the series studied, all of whom complained of pain after operation and requested relief: Nisentil was given to one-half these patients (239) and mep-

eridine to the other half. The dosage used was 30 to 60 mg. Nisentil and 50 to 100 mg. meperidine, on the basis that Nisentil is "approximately" twice as potent as meperidine. In both groups of patients more than a half stated that they had "marked" relief from pain, and over 90 per cent stated that they had had "marked or moderate" relief. While pain was relieved more rapidly with Nisentil than with meperidine, the duration of relief was shorter, so that the injections were given every two hours rather than every four hours as with meperidine. But the authors note that "psychologically" this may be of benefit to the patient, as many of the patients given Nisentil were pleased that they were getting medication for pain so frequently. The side effects observed were nausea and/or emesis and diaphoresis; nausea and vomiting occurred somewhat less frequently with Nisentil, and were less severe than with meperidine; diaphoresis, however, was more frequent and more profuse than with Nisentil. Nisentil did not cause euphoria, nor did it cause mental dullness, in which respects it is an improvement over other analgesic agents used postoperatively. Its lack of euphoric effect diminishes the danger of addiction to its use.

The Incidence of Postoperative Pancreatitis

J. H. Mahaffey and J. M. Howard (*A. M. A. Archives of Surgery*, 70:348, March 1955) report a study of the serum amylase concentration in 100 patients following abdominal surgery and 81 patients after operation other than laparotomy. Of the 100 patients after abdominal surgery, 27 showed a serum amylase concentration of 50 units or more (normal 15 to 40 units), and in 9 of these the amylase concentration was above 80 units. None of the 81 patients showed increased serum amylase concentration after other types of operation. These findings indicate that pancreatitis follows abdominal operations more frequently than is indicated by autopsy studies; only one of the 9 patients in this series who showed high amylase concentration died. The high incidence of pancreatitis following surgery of the duodenum, including operations on the common bile duct, indicates that this complication "rests on a mechanical basis." While the severer forms of postoperative pancreatitis can be correlated with the postoperative course, the milder forms may not be detected except by serial determinations of serum amylase concentration. Such determinations should be made, especially after operations involving the duodenum, not only "on an investigational basis," but also as a clinical aid in explaining complications following such surgery.

COMMENT

Many years ago Brocq postulated trauma as a factor in the causation of pancreatitis. Delicacy of dissection and gentleness in handling tissues about the duodenum will in many instances prevent a postoperative pancreatitis. Too many surgeons look at the clock when they operate and believe that excellency in surgery is rated by speed. In so doing they handle tissues roughly and dissect with the broad bold strokes of a painter imitating Picasso. At the same time they put hot laps over the pancreas and other abdominal organs; then a retractor is superimposed and a reluctant intern holds on to it for dear life. All these factors disturb an organ that has been resting quietly in its retroperitoneal hammock carrying on its normal functions. This trauma in some way is a precipitating factor in the production of pancreatitis. We have been able to produce pancreatitis in dogs experimentally by handling the pancreas in the manner mentioned above, i.e. by subjecting the

urgent to trauma of operation with retractors and hot laps. Of a certainty we cannot state dogmatically that all post-operative pancreatitis is due to these causes, yet there is no doubt that in many instances lack of gentleness may be a precipitating factor. B.J.F.

Tissue Sensitivity to a New Liquid Surgical Dressing

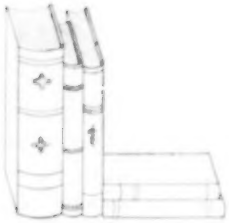
W. M. Lees and associates (*Annals of Surgery*, 141:281, Feb. 1955) report a study of sensitivity reactions to Aeroplast, a modified polyvinyl chloride resin in a solvent of ethyl acetate, developed at first as an emergency dressing for thermal burns, and later as a general surgical dressing. It is applied by spraying from an aerosol container with Freon®. Five test areas of the body were repeatedly sprayed with Aeroplast in 50 subjects (all women). Ten days after the last of these applications, a patch test of Aeroplast was applied to a forearm of each subject and protected with a gauze dressing; this area was inspected at twenty-four and forty-eight hours. There were no local skin reactions to the application of Aeroplast or to the patch test. White blood counts and eosinophil counts were made on all subjects during the period of Aeroplast applications. There was no significant change in the leukocyte count in any case. In 3 of the 50 subjects (6 per cent) some eosinophilia (up to 13 per cent) was found at some time during the period of study. If eosinophilia is "a dependable index" of tissue reaction, only 6 per cent of the subjects studied showed "any degree of sensitivity" to Aeroplast.

Subtotal Cholecystectomy in Acute Cholecystitis

G. F. Madding (*American Journal of Surgery*, 89:604, March 1955) has found the operation of subtotal cholecystectomy of value in cases of acute cholecystitis in which a total cholecystectomy cannot be safely done, especially in cases of acute suppurative or gangrenous cholecystitis in which the cystic duct and common bile duct are in "an edematous, friable and infected field." In this operation the gallbladder is dissected "in a retrograde fashion" from the surface of the liver to within 1 cm. of the cystic duct and all the stones are removed, especially the one causing obstruction of the duct. Four illustrative cases are reported in which this procedure gave good results and no further surgical procedure was required. In the author's opinion total cholecystectomy is the operation of choice in cases of acute gallbladder disease, but in some cases in which the total operation is not feasible, he has found subtotal cholecystectomy can be done, with much better results than cholecystectomy except in "extreme bad risk cases," in which only the drainage operation is indicated.

COMMENT

This report exemplifies a problem which confronts and has confronted many surgeons. What to do with a gallbladder that is so densely adherent to everything that even the mere motion of abdominal respiration many institute bleeding? The author offers his solution to the problem; another suggestion is electrocoagulation which can enable the surgeon to perform an obliterative cholecystectomy.



Medical Book News

Edited by Robert W. Hillman, M.D.

Cardiology

Das Elektrische Herzbild. Die Grundlagen Eines Neuen Elektrocardiographischen Verfahrens. By Dr. Wilhelm Ernsthausen in collaboration with Dr. Phil. Franz Kienle. Munich, Verlag für Biophysik Hermann Rinn, [c. 1953]. 8vo. 231 pages, illustrated. Cloth, DM 48.—

This new treatise on the electrical theory of the cardiographic investigation of heart is strictly for the specialist. The latter will find in it much new and valuable material. The long section on Fourier-analysis, for example, is not easy reading but is richly rewarding.

MILTON PLOTZ

Psychotherapy

Child Psychotherapy. By S. R. Slavson. New York, Columbia University Press, [c. 1952]. 8vo. 332 pages. Cloth, $4.50.

As its name indicates this book is intended as a clinical study, with special emphasis on the treatment of the emotionally disturbed and socially maladjusted child under twelve years of age.

Part One deals with the normal development of the child. It considers his psychobiological growth, his need for security and the influence of family, school and community on his personality development.

Part Two is concerned with psychopathology and Part Three with psychotherapy. Various types of therapeutic methods are considered. The chapter on group therapy for children is especially interesting, as this is debatable ground and the author, an authority on the subject, goes into detail as to its use.

For the physicians interested in the subject, this book is highly recommended.

STANLEY S. LAMM

Psychology

On the Nature of Psychotherapy. Basic Definitions and Assumptions for Students of Psychology and Medicine. By Arnold Bernstein. Garden City, N. Y., Doubleday & Co., [c. 1954]. 8vo. 36 pages. Paper, 85c. (Doubleday Papers in Psychology).

This book has the sub-title, *Basic Definitions and Assumptions for Students of Psychology and Medicine*. The author is instructor in psychology,

Important:

ROENTGEN MANIFESTATIONS of PANCREATIC DISEASE

By

MAXWELL HERBERT POPPEL, M.D.

Professor of Radiology
New York University
Post-Graduate Medical School

"The author presents all the facets in a most detailed and yet modest way. This is a very intelligent book, admirably combining radiology with anatomy, physiology, and pathology. Its illustrations are excellent."—*The Lancet*

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"In the complex problem of diagnosing pancreas affections the roentgenologist can be of valuable assistance to the clinician. Just what the roentgen methods are capable of achieving in this field has been compiled for the first time and is presented authoritatively and critically and at the same time concisely and completely in this volume."—*New York State Journal of Medicine*

406 pages 218 illustrations

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CHARLES C. THOMAS • PUBLISHER

Springfield, Illinois

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Professor Bernstein amply exemplifies commendable teacher ability. The wide range of contents is timely and discriminately formulated; fundamental definitions and principles of psychotherapy are in the foreground. Essential facts and factors underlying practice and theory of psychotherapy are categorically presented without attempting to teach specific psychotherapeutic methods.

The reader will enjoy this meaty digest of topics pertaining to magic, disease, therapy, psychosomatic continuum, somatogenesis, psychogenesis, sociogenesis, groups, patient's and psychotherapist's points of view, situational therapy, and psychology of the therapist. A list of books and papers for further reading adds to its value.

Issue may be taken with the author's delimitation of the qualifications of the psychotherapist. Psychotherapy is generally regarded as an important aspect of the medical specialty of psychiatry, although all physicians utilize it in varying degree. While non-medical persons may function in different auxiliary therapeutic roles, such should be under the direction of the medically qualified psychotherapist. The physician, by virtue of adequate education in the basic medical sciences and clinical skills essential for making diagnoses, selection, and formulation of methods of treatment, is entrusted by society with this weighty responsibility. The psychotherapist, should be in command of all the various usable factors, in the patient, in the environment, as in himself for optionally integrating and directing the treatment process.

The author is commended for this

splendid quasi-primer which clarifies a large number of areas of knowledge pertinent to the fuller understanding of the nature of psychotherapy.

FREDERICK L. PATRY

Pediatrics

Practical Fluid Therapy in Pediatrics. By Fontaine S. Hill, M.D. Philadelphia, W. B. Saunders Co., [c. 1954]. 8vo. 275 pages, illustrated. Cloth, $6.00.

In carefully analyzing this small volume one is struck with the simplicity the author has attained in bringing a usually hard-to-understand mechanism to useful everyday accomplishment. Anyone who attempts to keep abreast of the ever changing and often controversial opinions of the basic sciences, would find little difficulty in diagnosing what type of fluid therapy is needed at the bedside. The fluid balance and electrolytes are so flexible in the infant and young child that one must know promptly how much fluids and the proper electrolytes to apply to each situation. Thus the author has spelled out methods which can be used. Everyone who treats sick infants and children owes it to himself to understand the accurate needs of many of these very ill little patients.

This book will aid anyone desiring such information.

THURMAN B. GIVAN

Hematology

Sandoz Atlas of Haematology. Basle, Switzerland, Sandoz, Ltd., [c. 1949, 1952]. 4to. 91 pages with 44 color plates with explanations. Loose-leaf. Cloth, $7.00.

This atlas is far and away the best in the field. The photomicrographs are remarkably well done and show beautiful morphological detail of the various blood cells. Furthermore, the preparations that were photographed were very well selected and are free from artefacts. Every known hematological condition is well illustrated. The arrangement is excellent so that various cell types can be looked up very easily.

Any doctor or medical student who is interested in cell morphology should own a copy of this book.

R. JANET WATSON

Health Education

You and Your Health. By Edwin P. Jordan, M.D. New York, G. P. Putnam's Sons, [c. The Author, 1954]. 8vo. 296 pages. Cloth, $3.95.

This book is written for lay use and the material selected has been aimed at the most important aspects of the following: the heart, blood pressure and hardening of the arteries, the digestive system, cancer and related disorders, conquest of the infections, your body covering (skin, hair, nails), rheumatism, arthritis and related disorders, the allergies, the eyes and vision, the ears and hearing.

The chief purpose of this abridged outline is to cross the gap between what the physician would like to tell and what the patient and his friends would like to know. The context attempts to avoid any inclination of the patient to treat himself. Many of the chapters contain questions and answers at the end of the more formal discussion, some of which might seem unimportant to the physician. However, such items as dandruff and excessive hairiness, which are not ordinarily endangering to health, may be of great concern to the laity and

these require a certain amount of attention.

There are many helpful portions such as the recommendation of the Council on Physical Medicine and Rehabilitation for persons seeking a list of accepted hearing aids. In this case it is of course realized that a specialist would presumably have been consulted for a careful checkup.

The reviewer is not inclined to favor books on medical subjects for the laity, but most of the information seems to be reasonably accurate. Readers of this book will probably be particularly interested in the chapter on cancer and related disorders, in view of the high amount of publicity from the prophylactic point of view during recent years.

CECELIA JETT-JACKSON

BOOKS RECEIVED FOR REVIEW

Text-Book of Ophthalmology. By Sir Stewart Duke-Elder, M.D. Vol. VI. Injuries. St. Louis, C. V. Mosby Co., [c. 1954]. 8vo. Pp. 5,717/6,912. 1,145 illustrations, including 144 in color. Cloth, $25.00.

I Cured My Cancer. By Mary Payne, R.T. New York, Vantage Press, [c. 1954, The Author]. 8vo. 69 pages. Cloth, $2.50.

Financing Hospital Care In The United States. Edited by Harry Becker. Volume 2. Prepayment and the Community. New York, The Blakiston Division, McGraw-Hill Book Co., [c. 1955]. 8vo. 356 pages, illustrated. Cloth, $4.50.

PUBL. AUG. 1954 ◄——► 2ND EDITION

LEGAL MEDICINE

PATHOLOGY AND TOXICOLOGY

By THOMAS A. GONZALES, M.D., MORGAN VANCE, M.D., MILTON HELPERN, M.D., and CHAS. J. UMBERGER, Ph.D.

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1. Greenstein, L., and Sapirstein, M. R.: A. M. A. Arch. Neurol. & Psychiat. *70*:469 (Oct.) 1953. • 2. Smith, B., and Forster, F. M.: Neurology *4*:137 (Feb.) 1954. • 3. Smith, B. H., and McNaughton, F. L.: Canad. M. A. J. *68*:464 (May) 1953. • 4. Whitty, C. W. M.: Brit. M. J. *2*:540 (Sept. 5) 1953. • 5. Doyle, P. J., and Livingston, S.: J. Pediat. *43*:413 (Oct.) 1953. • 6. Timberlake, W. H., Abbott, J. A., and Schwab, R. S.: New England J. Med. *252*:304 (Feb. 24) 1955.

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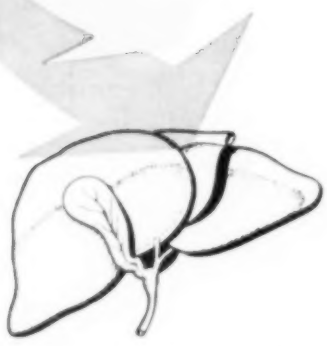

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1. Eisfelder, H. W., Am. Pract. & Dig. Treat., 5:778 (Oct.) 1954.

2. Sebrell, W. H., Jr., J.A.M.A., 152:42 (May) 1953.

3. Sherman, R. J., M.D., Medical Times, 82:107 (Feb.) 1954.

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THE CURRENT BUSINESS OUTLOOK

The first half of 1955 is now in the records as the best six months that business has ever had. It seems probable that the second half may be equally high or higher. Despite seasonal decline of automobile industry activity in the July-September quarter, the economy does not appear vulnerable to sympathetic weakness in other areas except for some normal summer dullness. The cyclical excesses which ordinarily appear after a period of boom times are not visible. Inventories are in line with sales, and sales are being well maintained. Unemployment is at the lowest point in a year and a half—on a seasonally adjusted basis—and employment and hours of work are relatively high. Price stability has continued and, due to the automobile and steel industry wage settlements, a faint air of inflation is now developing. Some of the favorable factors underlying the second half outlook include a rising trend of plant and equipment spending, a further upturn in personal income, and the anticipation of tax cuts in 1956.

New Production Records Record breaking activity so far this year marked up the Federal Reserve Index of Industrial Production to a new high of 139 in June. The best previous output was in May and July of boom year 1953. Significant contributors to rising activity have been the automobile, steel, and construction industries. These and allied manufacturers have been behind the surge in lumber, paperboard, and electric power production that has raised business activity to record levels. In the automobile industry, the first half of the year shows the phenomenal production pace of about 4¼ million cars, the highest in history. Housing starts have been second only to the record year of 1950

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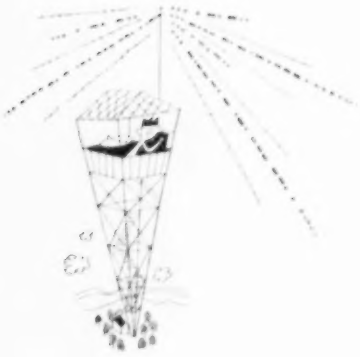

and at a rate indicating about 1,300,000 starts for the year. Heavy construction contract awards have been consistently high. The result has been active steel demand with production near capacity throughout the second quarter.

Auto Sales and Dealer Stocks

With fears of serious interruption to business activity cancelled by the auto and steel wage settlements, the economy is now at the point of testing the solidity of the present boom. Probably some second quarter activity was due to fears of strikes or was in anticipation of price rises to come. This latter factor may be a supporting element in the case of automobiles. If 1956 models have higher prices (as has been warned), the clearing of 1955 models from dealers' showrooms may be speeded. At any rate present inventories of almost 700,000 cars, or more than a month's supply at record sales rates, constitute a problem. Automobiles are one of the few areas where inventories have increased despite high sales. Although production is dropping off in anticipation of the late third quarter shift to new models, sales are also declining as the industry moves from its high spring selling period to the normally less active warm weather months.

Consumer credit relationships further complicate the auto and business picture. The proportion of automobiles bought on time is relatively high and increasing. Estimates vary between 65 and 75 per cent. Total consumer credit has been climbing sharply after a period in early 1954 when repayments exceeded new credit. The recent pace has been better than half a billion dollars of new credit per month. More than three-quarters of this has been automobile paper. So continuation of high automo-

like sales throughout the rest of the 1955 model year and into the 1956 year apparently also means a continuing growth in installment credit. In 1950 and again in 1952-53, periods of sharp rises in installment credit were followed by periods of debt repayment. This is economically good, since consumer solvency is maintained, but it also threatens a reduced rate of sales in some future time period. It seems probable, however, that with record sales so far in 1955 and the introduction of new models likely to spark sales again in the last quarter, this credit element may not begin limiting sales until 1956.

Mortgages and Housing The continuing growth of private debt may also have some repercussions in the building industry. Mortgage debt is continuing to grow. Most new homes continue to be financed through F.H.A. or V.A. channels. Although both these agencies are reportedly taking a closer look at loan applications, housing starts have declined only slightly. The main argument against tightening of credit policies is that a building slow-down would have unfavorable effects on the rest of the economy. Moreover, the political danger of upsetting the continuing boom is obvious. And the experience of 1954, despite the confidence that now appears everywhere, is no secure insurance that all the keys to stopping cyclical downturns have been found. Yet so far as housing is concerned, a rate between 1,000,000 and 1,500,000 starts per year is at a replacement rate of only 2 to 3 per cent a year, with little allowance for the new housing needs of a growing population.

No serious weakness appears to mar the present picture. Apart from the seasonal downturns developing in automo-

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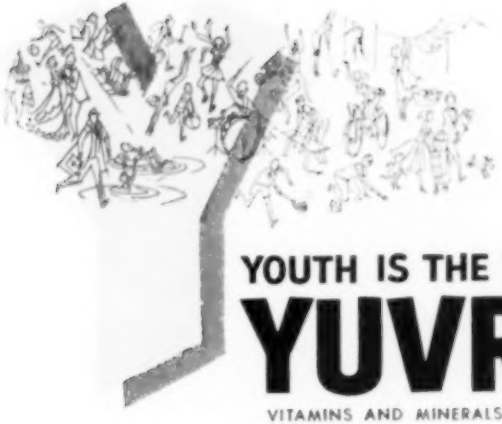
bile and housing and the potentially dangerous credit structure underlying both industries, the economy appears unusually strong. The decline in farm income may be leveling off, and on a per capita basis the average farmer is as well off as before since there are fewer farmers. The steel industry is apparently booked to near capacity by other industries, such as the freight car builders, to whom the boom has finally spread. And other industries have also been touched by the spark of continuing high retail sales. Department store sales, for instance, are 6 per cent ahead of 1954. The effect has been to keep new orders high, and production rates steady and rising, and yet to create no relative build-up in inventories. At the low point, manufacturers' inventories were $42.9 billion. Now they equal $43.6 billion, up only $700 million. Sales meanwhile have moved from a low of $22.5 billion to the present level (May) of $26.2 billion, up $3.7 billion. Despite record production, inventories are in line and have shown little tendency to climb at a rate faster than sales.

Employment Gains Labor statistics give the same generally favorable indications. Total employment of 64.0 million in June was 3.3 million more than it was in December and 1.9 million more than in June a year ago. Unemployment has dropped from a seasonal high of 3.4 million down to 2.7 million. The latter figure is only slightly above the unemployable base, which is probably near 2,000,000. In the durable goods manufacturing industries, hours worked of 41.7 per week are at the highest level since early 1953. Usually hours worked give advance indication of changes in activity as overtime is reduced before workers are laid off.

The combination of high employment and high hours worked, high production yet relatively low inventories because of high sales, is also behind the move of Gross National Product above the 1953 high water marks. For the second quarter of 1955, estimates run close to $380 billion compared with $375 billion in the first quarter, which in turn was substantially above the 1953 peak. Components of Gross National Product show mixed trends, but the important aspect is that no significant declines are in the offing and spending in the consumer part of the economy shows few signs of slowing down. To a record personal income rate of $301 billion in May may be added the benefits of recent wage settlements as well as those still to come. In addition there is a rise of government workers' income in the neighborhood of $1 billion per year. And Congress is now considering raising the minimum wage to either 90 cents or one dollar. It also seems a foregone conclusion that in the election year of 1956, both parties will be eager to pass some form of tax-cut affecting either individuals or corporations or possibly both. Whatever the amount of the cut, it should add to total spending.

Plant Expansion In the corporate spending segment of GNP, capital spending for plant and equipment is also scheduled to be increased. Outlays in the third quarter are planned at $28.3 billion, equal to the previous peak rate of the third quarter in 1953.

The beginning of a third phase of plant and equipment expansion has raised some doubts about its economic soundness. The short-run effect, of course, is plainly favorable. Such action indicates an optimistic viewpoint by business men and increases total spend-



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Chase Manhattan	108	2.20	49¼a	21¼a	53½	47a	52	4.2
Continental Oil	22	2.80	75½	14⅜a	90¾	70	83	3.4
First Natl. of Boston	92	2.70	65	44	67	54½	63	4.3
General Foods	34	3.00	80⅛	34	86⅛	75	81	3.7
Gulf Oil	20	2.00g	67½	24¾a	89⅞	61½	83	2.4g
Mercantile Trust	27	2.40	65a	38⅝a	65	56¾	65	3.7
Minn. Mng. & Mfg.	40	1.60	90	7½a	115	80	107	1.5
National Dairy	32	1.60	44¾a	12¼a	43⅝	37½	42	3.8
Pacific Gas & Elec.	37	2.20	48¼	29¾	52¼	44½	51	4.3
Standard Oil N. J.	74	5.00	112¼	28a	141½	106⅝	134	3.7
Union Pacific	56	7.00	154	54⅝a	178	139	162	4.3
LIBERAL INCOME								
Brooklyn Union Gas	7	1.80	33⅝	7⅞a	36½	32¼	33	5.5
Chesapeake & Ohio	34	3.00	66⅞	25	54¾	42½	52	5.8
Gen. Public Utilities	10	1.70	34⅞	10⅞	37¼	33	36	4.7
Glidden Co.	23	2.00	48½	12⅝a	44½	38½	40	5.0
International Nickel	22	3.00m	59½	23⅛	74⅛	57⅛	73	4.1m
Interstate Power	8	0.70	14	5¾	14⅝	12¾	14	5.0
Pub. Serv. El. & Gas	32	1.60	29¾	20	33¼	28½	33	4.8
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Eastern Air Lines	6	1.00	40	9¾a	58	35¼	52	1.9
Household Finance	39	1.20	33a	9¾a	31⅜	28	29	4.1
Lehigh Portland	20	1.60	60¼	14⅝a	74½	53⅛	69	2.3
Pepsi Cola	4	0.80	40½	7½	23⅝	17⅞	23	3.5
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Sinclair Oil	22	2.60	52⅜	14	59¾	48½	57	4.6
Skelly Oil	19	1.80	54⅞	7a	57½	48½	56	3.2
Standard Brands	57	2.15	55	17¼	40⅞	36⅝	40	5.4
Texas Utilities	39	2.32	66	19⅝	79	61	74	3.1
Transamerica	22	1.40	40⅞	10	48⅜	37⅛	46	3.0
United Fruit	57	3.00	73⅝	36	60	51⅛	57	5.3
United Gas Corp.	11	1.50	35	9¾	35½	31⅜	32	4.7
Wash. Water Pwr.	56	1.70	36¼	24	41¾	32	41	4.1
SPECULATIVE								
Armour & Co.	—	Nil	18½	5	16⅜	13½	15	—
El Paso Nat. Gas	20	2.00	41¾	11⅜a	54½	39¾	47	4.3
Gulf Interstate Gas	1	0.50	11½	5⅛	14½	10¼	12	4.2
Intl. Tel. & Tel.	5	1.20	33	7½	30	23¾	29	4.1
Northern Pacific	13	3.00	94⅜	11½	83⅓	64⅞	78	3.8
Radio Corp.	15	1.35	39¼	7⅓	55⅜	36¾	50	2.7
Reynolds Metals	14	1.50g	125	9⅞a	222¾	109½	215	0.7g
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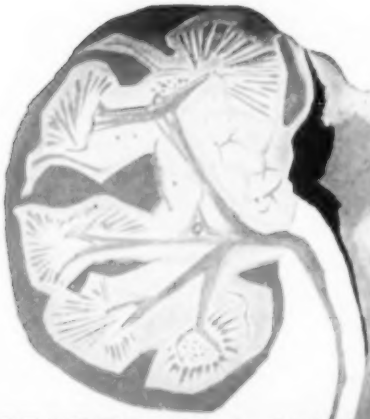

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ing. But the longer term impact may be different. We may be over-expanding our producing facilities and creating danger of overcapacity in the years ahead.

In view, however, of the long period of time from 1930 until after the end of World War II when spending for plant and equipment was extremely low, it seems doubtful that overexpansion has yet developed. Post-war economic growth has been more spectacular than almost anyone dreamed. Plant capacity is strained almost to the limit in many industries whenever business is good. And a case can be made for the competitive necessity of continually erecting new plant and installing new equipment in order to compete effectively. The decision almost has to be to retire old equipment rather than to forego new spending.

Meanwhile, government spending for defense has stabilized at a rate of about $40 billion per year. Little change seems probable despite hopes for armament reduction as a result of "Summit" talks this summer. The race for air supremacy has, if anything, been quickened by Soviet accomplishments. In fact, technical, electronic, and other changes arising from the use of atomic and jet propulsion and nuclear weapons have speeded obsolescence and the need for replacement of existing equipment in all military and naval fields. Since housekeeping expenditures form a large proportion of the $40 billion total, it is unlikely that total expenditures for the military will drop below present figures.

Umm-m-m-m-m-m... tastes like banana-flavored

Com

The Rest of the Year In summarizing, there are strong and continuing forces that appear to underlie the present boom. The second half of the year should be more stable than the first six months, in which the rise was steep. Seasonal declines in automobile and housing activity are likely to be matched by strength in some of the lag sectors of the economy and by a continuing rise in Gross National Product. The housing boom, despite worries about its character, seems built on conservative ideas of replacement in view of our sharply rising standard of living. Even the high pace of automobile output is not far out of line if one considers the total number of family units and the growing number of two- and even three-car families. These facts appear to spell out a firm base for continued growth but do not allow for sharp changes in attitudes or expectations or for weaknesses that have not yet shown up in our business cycle experience. Considering the advanced stage of the present boom, the belief that business can only become more active is always a dangerous one to cultivate.

Optimal Diuretic Effect is Daylong

In maintenance therapy of congestive failure, as in treatment of diabetes, the optimal effect is daylong. It does not permit the alternation of Na and fluid output followed by Na and fluid reaccumulation, even within a 24-hour period, according to an article in the *Diuretic Review*.

pocillin®

(HYDRABAMINE PENICILLIN G)

New Ready-Mixed Penicillin Suspension

Upjohn

Physicians Find New Way To Ease High Cost Of Raising Children

Reversionary Trusts

RANDOLPH SCOTT*
New York, New York

Until quite recently, a well-to-do surgeon and his wife whom, for the purposes of this article, I shall call Dr. and Mrs. Jones, had, in addition to providing for her support and maintenance, been giving their teen-age daughter an allowance of $50.00 a month.

Since their joint income put them in a 50 per cent tax bracket, it required about $100 in income each month to make such an allowance possible. On an annual basis, $1200 in earnings was necessary to provide this $600 yearly allowance.

Early this year, the couple tried a new approach. Dr. and Mrs. Jones set up a $12,000 trust fund for their daughter and invested the trust principal in mutual fund shares geared to yield a 5 per cent annual return.

$12,000 at 5 per cent means a yearly income from the principal of $600—or exactly the amount Dr. and Mrs. Jones had been in the habit of giving their daughter each year. But with one major difference:

It is tax-free.

If this comes as a surprise to you, if you now find yourself asking aloud, "Why haven't I heard about this before?" you will be relieved to know that the idea is new, that comparatively few persons, physicians included, have had an opportunity to take advantage of it because it *is* new, and that there is no reason in the world why you cannot apply it to your own family financial needs.

Dr. and Mrs. Jones were among the first to reap the financial advantages of a tax-savings device which became statutorily possible last January 1st with the passage last Fall of the new Internal Revenue Code—the Reversionary Trust Fund.

The Reversionary Trust is, in effect, a new device similar to the tax-free gift trust, but with one important protection for the grantor if he cannot afford to part permanently with a large portion of

*Founder and Head of the New York City Investment Firm of Randolph Scott & Co., Inc., 115 Broadway.

the doctor depends on the tailor for clothes

the tailor depends on the doctor for health

both depend on the farmer for food

There is a basic principle of interdependence which occurs in almost every phase of life. It exists in nutrition, too, where the various dietary elements form part of a vast interrelated structure.* This concept has been carefully observed in the formulation of "Clusivol" for multiple vitamin-mineral supplementation.

"CLUSIVOL"®

provides all vitamins and minerals known to be essential for balanced nutrition—also other accessory food factors and trace elements believed to be significant.

The average daily dose (2 capsules) provides:

Vitamin A (synthetic)	25,000	U.S.P. Units	Biotin	0.1	mg.
Vitamin D (irradiated ergosterol)	2,000	U.S.P. Units	*dl*-Methionine	20.0	mg.
Vitamin C (ascorbic acid)	150.0	mg.	Cobalt — from cobalt sulfate	0.1	mg.
Thiamine mononitrate (B_1)	10.0	mg.	Copper — from copper sulfate	1.0	mg.
Riboflavin (B_2)	5.0	mg.	Fluorine — from calcium fluoride	0.025	mg.
Pyridoxine HCl (B_6)	1.0	mg.	Iron — from 4 gr. ferrous sulfate exsic.	76.2	mg.
Panthenol, equivalent to of calcium pantothenate	10.0	mg.	Calcium — from dicalcium phosphate	165.0	mg.
			Manganese — from manganous sulfate	1.0	mg.
Vitamin B_{12}	2.0	mcg.	Iodine — from potassium iodide	0.15	mg.
Folic acid U.S.P.	2.0	mg.	Molybdenum — from sodium molybdate	0.2	mg.
Nicotinamide	100.0	mg.	Potassium — from potassium sulfate	5.0	mg.
Vitamin E (as mixed tocopherols natural)	10.0	mg.	Zinc — from zinc sulfate	1.2	mg.
Inositol	30.0	mg.	Magnesium — from magnesium sulfate	6.0	mg.
Choline — from choline bitartrate	30.0	mg.	Phosphorus — from dicalcium phosphate	127.4	mg.

No. 293—supplied in bottles of 100 and 1,000.

*Waife, S.O. M. Clin. North America 33:1709 (Nov.) 1949.

in Stress Conditions - in Obesity - in Chronic Disease

5564

Ayerst

his savings—he gets his money back after ten years.

Here is how it works, here is how you can more easily contribute more to the support of your youngsters without putting a crimp in your future financial requirements:

You establish a Reversionary Trust in the name of your child or children under the regulations of the 1954 Internal Revenue Code.

Then, your youngsters enjoy the income from this trust for a period of ten years or more, after which the trust principal comes back to you—as if you had never parted with it.

According to the amended tax law, you may draw on the earnings of such a trust for their support—and still retain the standard $600 exemption for each child, provided those earnings amount to less than half of the total cost of his support.

You are not limited to one trust. You can set up any number of them for different minors—provided, of course, they run at least the full ten-year period.

Dr. and Mrs. Jones' main objective in establishing a Reversionary Trust was to provide a tax-free monthly allowance for their daughter. Actually the Trust income can apply to a wide range of personal situations.

For example, let us apply the Reversionary Trust concept to another doctor who estimates it would take, say, $10,000 to provide his son with the training he would need from his entrance into medical school until the day he enters private practice. Assume the doctor is in a pretty high tax bracket—60 per cent.

If he were to invest $30,000 for this purpose in Series E bonds for ten years, his return, at 3 per cent and at the 60 per cent tax rate, would come to only $360 a year. This amount certainly wouldn't take the young man very far into his medical training, tuition rates and living expenses being what they are these days.

And so, he by-passes the Government Bonds method—for this purpose, at least—and he elects to establish a Reversionary Trust with his $30,000. Let us say he wants the trust principal to be invested conservatively — in issues geared for a 4 per cent return.

This would bring in a yearly trust income of $1200. At the end of the ten-year period—which can be extended if the situation warrants it—the accumulated earnings from this particular trust would total $12,000 without including benefits of compounding.

This figure amounts to a net gain, over the ten-year income from Series E bonds, of $3,400. More important, it would go far towards financing tuition and living expenses during the son's medical training.

Of special importance to families whose incomes may not begin to approach the 50 or 60 per cent brackets is the fact that Reversionary Trust Funds can have a practical application to taxpayers whose taxable income is as low as $15,000 a year.

Just to illustrate how effectively Reversionary Trusts can apply to more modest incomes, it might be worthwhile to include here a hypothetical case.

Dr. Smith's annual income after deductions, but before taxes, comes to $15,000. He decides to take $7,500 out of his savings account and invest it in such a way that its earnings, compounded over ten years, will contribute to the future support of his child. He selects investments calculated to give him a 5 per cent return.

FOR SUPERIOR PERFORMANCE—

in Antibiotic Therapy— **POLYCYCLINE**
a tetracycline produced by a unique process of direct fermentation

BRISTOL LABORATORIES INC.
SYRACUSE, NEW YORK

FOR SUPERIOR PERFORMANCE IN ANTIBIOTIC THERAPY

—effective, safer, more sustained action with this newest broad-spectrum antibiotic

Polycycline – available in many dosage forms – affords significant clinical advantages in broad-spectrum antibiotic therapy:

Effective in broad range

– against Gram-positive and Gram-negative organisms, certain rickettsiae and large viruses.

Greater tolerance

– markedly lower incidence and severity of adverse side effects.

Greater solubility

– than chlortetracycline, yielding quicker absorption and increased diffusion in body fluids and tissues.

Greater stability

– in solution than chlortetracycline or oxytetracycline, assuring higher, more sustained blood levels.

•

Polycycline is a tetracycline produced by the unique Bristol process of direct fermentation. Its basic structural formula is free of a chlorine atom (present in chlortetracycline), and of an hydroxyl group (present in oxytetracycline).

Your pharmacist has all dosage forms of Polycycline available for your prescription:

POLYCYCLINE
SUSPENSION WITH TRIPLE SULFONAMIDES

Coconut oil suspension of tetracycline with three sulfonamides. In concentration of 125 mg. tetracycline HCl with 167 mg. each of sulfadiazine, sulfamerazine and sulfamethazine per 5 cc.; in bottles of 2 fl. oz.

POLYCYCLINE
AQUEOUS '250' or AQUEOUS '125'

An aqueous suspension ready to use without reconstitution. Stable for 18 months without refrigeration. Highly palatable, cherry flavor. As calcium tetracycline equivalent to 250 mg. (or 125 mg.) tetracycline HCl per 5 cc.; in bottles of 1 fl. oz.

POLYCYCLINE
SUSPENSION '250'

A really palatable oil suspension, requiring no dilution or reconstitution. Needs no refrigeration – stable for 18 months. In concentration of 250 mg. tetracycline HCl per 5 cc.; in bottles of 1 fl. oz.

For accurate dosage in small amounts. In concentration of 100 mg. tetracycline HCl per cc.; in bottles of 10 cc. with dropper calibrated for administration of 25 mg. or 50 mg.

POLYCYCLINE
PEDIATRIC DROPS

POLYCYCLINE
AQUEOUS PEDIATRIC DROPS

As calcium tetracycline equivalent to 100 mg. tetracycline HCl per cc. in bottles of 10 cc. with dropper calibrated at 25 mg. and 50 mg.

Handy form for oral use, in two potencies of tetracycline HCl. In capsules of 100 mg.; in bottles of 25 and 100. In capsules of 250 mg.; in bottles of 16 and 100.

POLYCYCLINE
CAPSULES

For deep intramuscular injection. In single-dose vials of 100 mg. tetracycline HCl per vial.

POLYCYCLINE
INTRAMUSCULAR

POLYCYCLINE
OINTMENT
WITH 2% XYLOCAINE*

–30 mg. tetracycline HCl with 20 mg. Lidocaine (as the base), per gram.

POLYCYCLINE
OPHTHALMIC OINTMENT
WITH 2% XYLOCAINE*

–10 mg. tetracycline HCl with 20 mg. Lidocaine (as the base), per gram.

When you think of Tetracycline, think of

Bristol
LABORATORIES INC.
SYRACUSE, NEW YORK

POLYCYCLINE®

(Tetracycline HCl Bristol)

BUTIBEL*

combines tension-relieving Butisol® Sodium with spasm-relaxing natural belladonna

...both agents have approximately equal durations of action (no overlapping sedation or inadequate spasmolysis).

...less danger of accumulation or development of tolerance from Butisol Sodium—even with frequent, prolonged use.

Each tablet or 5 cc. (one teaspoonful) of Butibel represents:
Butisol Sodium 10 mg. (⅙ gr.)
Ext. Belladonna 15 mg. (¼ gr.)

McNEIL
LABORATORIES, INC.
Philadelphia 32, Pa.

*Trade-mark

Being in a 24 per cent tax bracket, Dr. Smith's first-year earnings, at 5 per cent, would come to $375 minus 24 per cent, or a total of $285. Compounded four times a year for ten years, his original investment of $7,500 would earn $3200 —probably a little less.

But if he elects to take that same $7,500 and use it to establish a Reversionary Trust whose principal is invested in Mutual Funds, at the same rate of return, he could expect to earn about $4200 over the ten-year period. This represents a gain of $1000 over the non-trust investment plan—a sizable amount of cash even in these days.

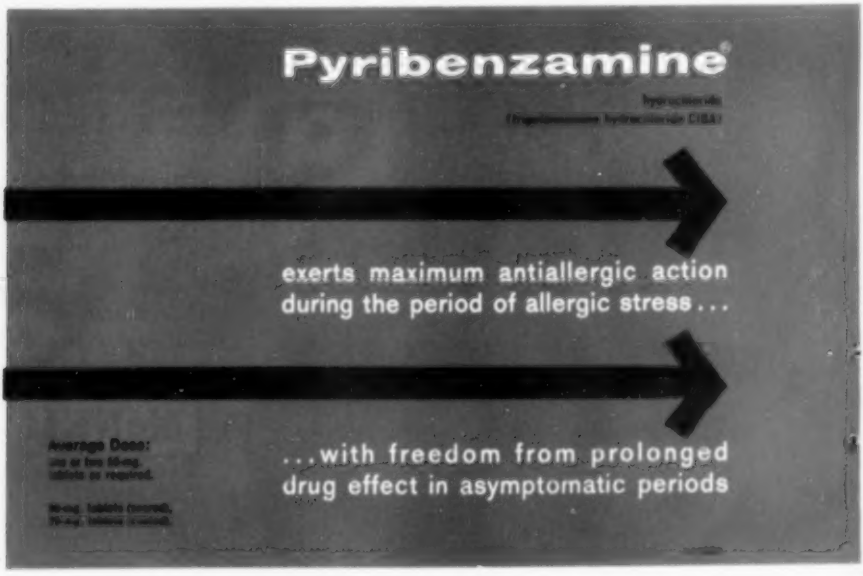
One word of caution: Should you decide to establish one of these trust funds, be sure you have the trust agreement drawn up by an attorney who specializes in tax and trust work. In all likelihood your investment man's legal counsel would have this background and ...not be willing to draw up the necessary papers for a reasonable fee.

Although there are no inflexible rules regarding how the principal of these trusts should be invested, the writer believes that MUTUAL FUNDS are the ideal medium.

As you may know, mutual funds are, in effect, the investor's investor. An investment in Mutual Funds automatically makes the shareholder an investor in literally dozens of different securities. The three built-in features of mutual funds — management, supervision and diversification — serve to provide greater protection, steadier, more consistent income and considerably less risk than would be the case with direct investment in a relatively few corporate securities.

Moreover there are a great variety of Mutual Funds to choose from, providing income from a wide range of companies.

For example, there are ultra-conserva-



tive funds investing only in top-rated bonds; there are balanced funds investing in a great variety of securities; common stock funds with probable protection against inflation; funds interested in only one type of industry, etc.

In setting up a Reversionary Trust for their daughter, Dr. and Mrs. Jones would obviously be seeking to invest its principal in a fund or funds likely, on the basis of past performance, to provide an income of about 5 per cent. The other doctor cited in this article would, of course, want the principal of his son's trust invested in funds designed to yield about 4 per cent annually.

Mutual Funds as an investment medium for Reversionary Trusts offer these specific advantages: (1) broad diversification, (2) expert management and supervision, (3) minimum risk, and (4) maximum opportunities for necessary and consistent income.

These four specific advantages add up to one general one: peace of mind. Day-to-day market conditions are not likely to have any material effect on your dividend earnings, nor on the actual cash value of your fund shares. You will never suffer the unhappy experience of becoming "married" to your investment.

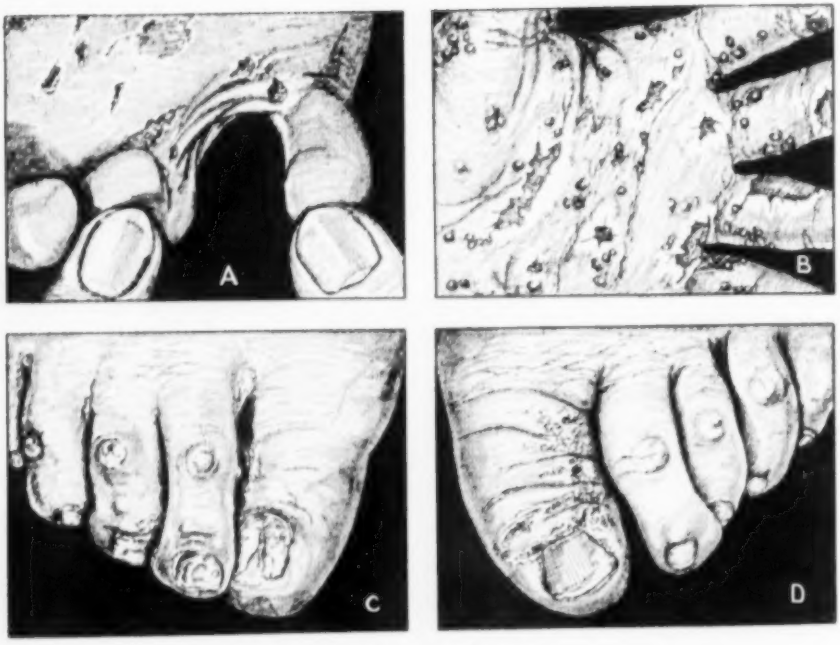
In bringing this article to a close, I would say that Reversionary Trust Funds —especially those which employ mutual funds—are certainly one of the most salutory additions to the new Internal Revenue Code.

Whether you establish one or more in favor of your son or grandson, daughter or grand-daughter, niece or nephew, whether your aim is to provide a tax-free method of contributing to their support, or to their future education—or even to their monthly allowance—trusts can ease many a financial burden for you.

In more than thirty years in the in-

vestment field. I have seldom come upon a tax-savings device which applies so broadly to so many families in so many different ways.

Clini-Clipping



Tinea Pedis

A. Inflammatory type showing interdigital maceration between 4th and 5th toes.

B. Dermatophytide of hand associated with Trichophyton gypseum infection of feet.

C. Chronic type caused by Trichophyton purpurea showing yellow, opaque, brittle involvement of toenails.

D. Secondary pyogenic invasion of the tissues in the acute inflammatory type when the term eczematoid ringworm may be appropriately used.

PRONEMIA*

Hematinic Lederle

the most potent of all oral hematinics

One capsule daily for treatment and maintenance of *all* treatable anemias, including pernicious anemia.

Each capsule contains: Vitamin B_{12} with Intrinsic Factor Concentrate . . . 1 U.S.P. Oral Unit; Vitamin B_{12} (additional) . . . 15 mcgm.; Powdered Stomach . . . 200 mg.; Ferrous Sulfate Exsiccated . . . 400 mg.; Ascorbic Acid (C) . . . 150 mg.; Folic Acid . . . 4 mg.

Lederle

LEDERLE LABORATORIES DIVISION *American Cyanamid Company* Pearl River, New York

*Reg. U.S. Pat. Off.

MODERN THERAPEUTICS

Antibiotic-Cortisone Therapy in Resistant Pelvic Infections

A combination of antibiotic therapy with cortisone produced good results in each of 10 women with resistant pelvic infections, according to a report by Hurtig in *Canadian Med. Assoc. J.* [72:123 (1955)]. Without this therapy, three of the women would have died and morbidity would have been prolonged with radical surgery inevitably following in the others.

Pyogenic Skin Diseases Respond to Oral Tetracyn

A variety of pyogenic dermatoses in 145 patients was "easily and promptly" controlled by orally administered Tetracyn, according to Dr. Lawrence C. Goldberg, of this city.

Dr. Goldberg reports on his study in a recent issue of the *A.M.A. Archives of Dermatology* [71:633 (1955)].

Tetracyn controlled infections of the skin in such diseases as impetigo contagiosa and the pustular phase of acne vulgaris, rosacea and necrotica, folliculitis, impetiginized dermatoses, infectious eczematoid dermatitis and hidradenitis.

According to Dr. Goldberg, Tetracyn also cured chancroid and prevented infection in severe secondary burns.

The physician found that Tetracyn was tolerated at higher levels than Terramycin or Aureomycin and produced a minimum of side-reactions such as nausea, vomiting and diarrhea.

Of the 145 patients studied by Dr. Goldberg, only a few complained of gastric distress and only one had nausea and vomiting.

Dr. Goldberg reported that Tetracyn is not only of value in the treatment of the dermatoses observed in this trial, but should also be tried in other similar skin ailments.

Levarterenol Bitartrate Effective in Surgical Shock

Levarterenol bitartrate (Levophed) was effective in relieving hypotension due to surgical shock in 16 of 19 patients. The degree of response was related to the cause of collapse. The best results were obtained in peripheral vascular failure uncomplicated by blood loss. In such cases there was an immediate and dramatic rise in the systolic blood pressure. Satisfying results were

—Continued on page 108a

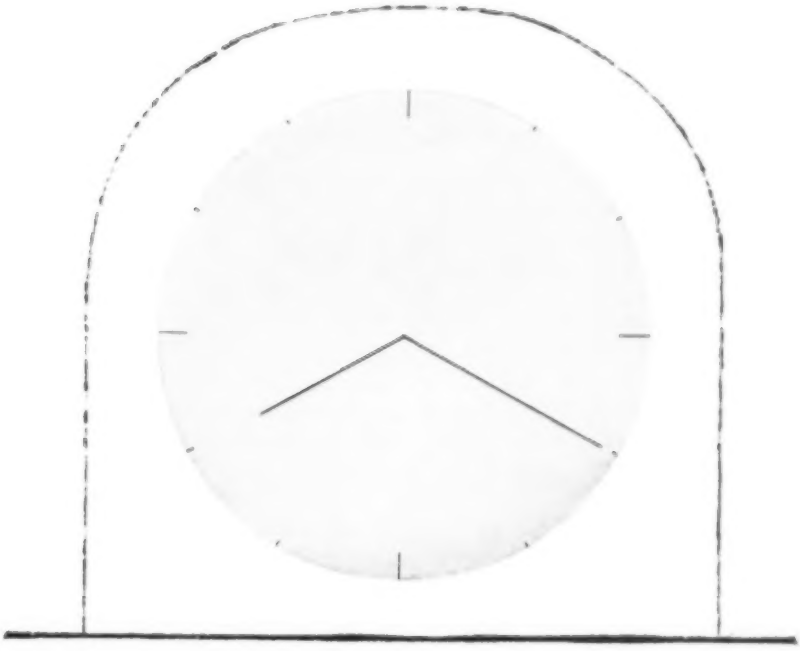
Diagnosis, Please!

ANSWER

(from page 25a)

ESOPHAGEAL VARICES

Numerous serpigenous intraluminal filling defects which change on Muller and Valsalva Maneuvers.



round-the-clock antihistamine protection

Green writes: "Last year I obtained for investigational use, the antihistamine chlorprophenpyridamine maleate, so prepared . . . that its resultant therapeutic effect was designed to last approximately twelve hours following the administration of a single oral dose."

After giving this preparation ("Teldrin" *Spansule* capsules) to 357 allergic patients, Green reported:

"The results . . . confirm the postulated long-acting property and low side effect liability of ["Teldrin" *Spansule* capsules]."

Green, M.A.: Ann. Allergy *12*:273

Teldrin*

chlorprophenpyridamine maleate

Spansule*

sustained release capsules, S.K.F.

Antihistamine

In 2 dosage strengths:
8 mg. (1 dot on capsule) &
12 mg. (2 dots on capsule)

One "Teldrin" *Spansule* capsule q12h provides 24-hour uninterrupted, sustained antihistamine protection from a wide range of allergic manifestations.

made only by

Smith, Kline & French Laboratories, Philadelphia

first in sustained release oral medication

*T.M. Reg. U.S. Pat. Off. Patent Applied For

—Continued from page 106a

also obtained in cases of pre-operative shock subsequently successfully subjected to major surgery.

Writing in *Brit. J. Anesth.* [27:31 (1955)], Shanahan stated that probably the ideal method of combatting shock is the simultaneous administration of blood and levarterenol bitartrate. When blood is not available, the drug may tide the patient over a dangerous period.

Dermatoses Cleared by Tetracycline Ointment

Complete clearance of streptococcal and staphylococcal infections complicating various dermatoses was obtained by the use of a tetracycline ointment containing 30 mg. in each Gm. of a petrolatum base. Sixteen of 18 patients who had exhibited reactions to other antibiotics showed complete clearance of their infections when treated with the tetracycline ointment. There also appeared to be a low incidence of sensitization and a limited cross sensitization with other antibiotics, according to Welsh and Ede in *A.M.A. Arch. Dermatol.* [71:111 (1955)].

The ointment also appeared to have some antipruritic action. This was particularly evident in patients with atopic dermatitis and pruritis ani complicated by secondary impetiginous infections or folliculitis.

Neomycin Sulfate in the Treatment of Infant Diarrhea

Infant diarrhea caused by species of Shigella or Salmonella was treated with neomycin sulfate in a dosage of 50 mg. per Kg. per day for a period of five

—Continued on page 110a

The high degree of solubility of "Thiosulfil" combined with its high bacteriostatic activity and low acetylation rate insure rapid and effective action with virtually no side effects.

"THIOSULFIL"®

Brand of sulfamethylthiadiazole

safest, most effective sulfonamide for urinary tract infections

Ayerst Laboratories • New York, N. Y. • Montreal, Canada

5535

direct anti-edema anti-inflammatory agent

PARENZYME®

INTRAMUSCULAR TRYPSIN, solvent, purified, crystalline enzyme in Sesame Oil suspension

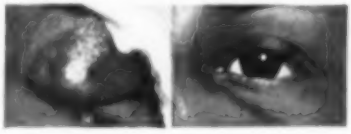
In local stress conditions—the physiological reaction is toward a *break through* to establish "metabolic continuity" and to mobilize the basic biology of resistance and recovery.

Clinical and experimental evidence demonstrates the superior effectiveness of a wide-range, direct-acting and proteolytic enzyme, such as trypsin, in the treatment of traumatic edema. PARENZYME is the only available preparation with a direct depolymerizing effect on the soft fibrin and other denatured tissue protein deposits forming a mechanical barrier around the injured area. Every physiologic restorative process present in the blood is made available for absorption of edema and necrotized tissue, lessening pain, reducing inflammation, and speeding the healing process.

CASE HISTORY

Deep laceration left eyebrow. Penicillin administered, condition worsened, marked edema, preauricular adenopathy, pain.

Antibiotics plus Parenzyme administered. 24 hour improvement; 48 hours eye opened. Rapidly healing.



in THROMBOPHLEBITIS PARENZYME

significantly reduces the incidence of pulmonary emboli, and initiates biochemical reactions resulting in prompt and sustained subsidence of the signs of acute inflammation: pain, edema, redness, Homan's sign, fever, elevated sedimentation rate, leukocytosis, and inability to walk.

advantages of PARENZYME INTRAMUSCULAR TRYPSIN

- **safe method of administering parenteral trypsin; no major side effects**
- **known amount of active enzyme is used**
- **no metabolic derangements such as often occur with other anti-inflammatory agents**
- **not anticoagulant**
- **early ambulation and return to full activity**
- **enhances use of antibiotic therapy**
- **can be used in conjunction with any other treatment you prescribe**

The cardinal indication for trypsin is acute inflammation, regardless of etiology. Other indications:

TRAUMATIC WOUNDS
slow-healing wounds
bruises
contusions
black eyes

SKIN ULCERS
decubitus
diabetic
varicose

VASCULAR DISORDERS
phlebitis
thrombophlebitis
phlebothrombosis

OPHTHALMIC
iritis
iridocyclitis
chorioretinitis

Write for literature and samples for clinical trial.

DOSAGE: 2.5 mg. (0.5 cc.) intragluteally q. 6 h. until improvement results; q. 12 h. thereafter **RECOMMENDED METHOD OF INJECTION:** Very slowly intragluteally **SUPPLIED:** 5 cc. multiple-dose vials (5 mg. trypsin/cc.)

A PRODUCT OF ORIGINAL RESEARCH

THE NATIONAL DRUG COMPANY PHILADELPHIA 44, PA.

—Continued from page 108a

days. Treatment was begun in 25 infants up to 4 months of age, within 4 days of the onset of illness. Supportive treatment with oral or intravenous fluids and dietary control was used as indicated.

Ponce de Leon stated in *Antibiotic Med.* [*1*:20 (1955)] that all but four of the infants responded favorably to this treatment. In one of the infants in whom therapy failed, typical typhoid fever developed. The other three had shigellosis.

Among the infants who responded favorably to therapy, there were no relapses and no indication of toxic effects from the antibiotic. The general physical condition of the infant played an important part in the rapidity of the response to treatment.

Encouraging Results with C.V.P. in Hemorrhagic Cystitis

Dr. C. C. Saelhof reports on a preliminary study in which a combination of water-soluble natural citrus bioflavonoids with ascorbic acid (C.V.P.) was used successfully as an anti-inflammatory agent in nineteen patients with hemorrhagic cystitis and trigonitis. [*Amer. J. Dig. Dis.* 22:204 1955]. The

—Continued on page 112a

NEW *combined*

anti-inflammatory – anti-infective

action

'CORTISPORIN' brand

POLYMYXIN B – BACITRACIN – NEOMYCIN WITH **HYDROCORTISONE 1%**

ointment

for ophthalmic and dermatologic use

- relieves erythema and edema promptly
- soothes itching
- kills virtually all bacteria likely to be found topically
- minimizes scarring and clouding of vision after corneal surgery

Each gram of 'CORTISPORIN' OINTMENT contains:

'Aerosporin'® Sulfate Polymyxin B Sulfate	5,000 Units
Bacitracin	400 Units
Neomycin Sulfate (equivalent to 3.5 mg. neomycin base)	5 mg.
Hydrocortisone (free alcohol)	10 mg. (1%)

Available in tubes of ⅛ oz. with applicator tip.

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, N.Y.

—Continued from page 110a

results of C.V.P. therapy "compare favorably" with those obtained with the sulfa preparation, sulfasoxazole. There were no side effects with C.V.P., but nausea and gastric irritability were frequent with the sulfonamide.

Urine cultures became negative and pus cells and red blood cells disappeared within five days, average. The well-being of the bioflavonoid-treated patients was more pronounced than those on the sulfonamide. The dosage of C.V.P. ("citrus vitamin P") was 2 or 3 capsules (each containing 100 mg. of bioflavonoid and ascorbic acid) at 8 A.M., 12, 4 P.M. and 8 P.M. for 3 or 4 days.

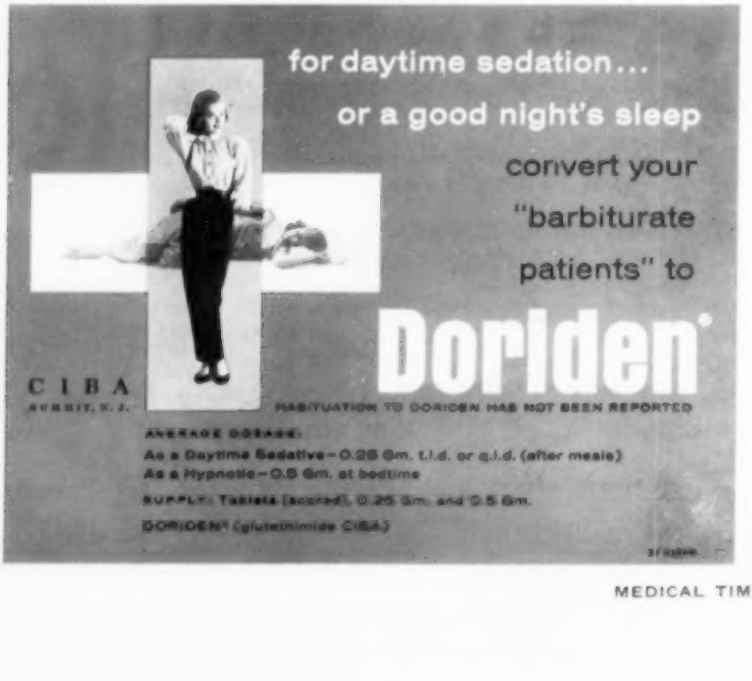
In inflammatory conditions of the bladder mucous membrane, according to the author, there is a localized capillary syndrome, with abnormal capillary permeability and bleeding. This promotes and aggravates bacterial infection and the inflammatory process. C.V.P. "drastically reduced capillary permeability" and the protein leakage into the tissues which occurs in inflammation.

Topical Urethral Anesthesia with Tripelennamine Hydrochloride

A 2 per cent solution and a 2 per cent jelly of tripelennamine hydrochloride proved to be effective in the production of topical anesthesia of the urethra in over 2000 urological cases, according to Fitzpatrick and Orr in *J.A.M.A.* [*158*:261 (1955)]. The total dosage should not exceed 300 mg. in adults.

A slight initial burning was noticed by a few patients but, otherwise, no untoward reactions were noted and there were practically no failures of anesthetic action. The interest in the use of antihistamines for topical anesthesia has

—Continued on page 114a



consensus of research is . . .

All hypertensives should receive the same initial therapy

The consensus of research clinicians advocates Rauwolfia alkaloids – such as Rautensin, a standardized extract containing *all* the hypotensive and tranquillizing Rauwolfia alkaloids, free from inert material – as the *first step* in all hypotensive therapy. The lack of toxicity over a wide range of dosage, the tranquillizing, headache-relieving, pulse-slowing and gradual hypotensive action of Rautensin make it one of the safest preparations in the initial treatment of all types of hypertension, irrespective of severity.

Then, too, your nervous, stress-ridden patients with *early labile hypertension* respond especially well to Rautensin. In the more stubborn cases requiring combination therapy Rautensin, used as a platform on which to build an effective regimen, usually permits reducing the dosage of other hypotensive agents. Result: Less side effects.

Each Rautensin tablet contains 2 mg. of purified Rauwolfia alkaloids (alseroxylon fraction).

Dosage: For the first 20 to 30 days 2 tablets (4 mg.) once daily before retiring; thereafter 1 tablet (2 mg.) daily usually suffices.

RAUTENSIN®

for basic therapy in all hypertensives

Rautensin is a DORSEY preparation

Smith-Dorsey • Lincoln, Nebraska • A Division of The Wander Company

—Continued from page 112a

developed because some patients show atopic reactions to the commonly used topical anesthetic agents.

Treatment of Severe Constipation with Dioctyl Sodium Sulfosuccinate

A 1 per cent aqueous solution of dioctyl sodium sulfosuccinate has proved to be effective in the treatment of certain types of constipation. It is particularly effective in fecal impaction associated with megacolon, anal fissure, postoperative anal atresia, and in bedridden patients of many types, including, patients convalescing from poliomyelitis and elderly invalids. According to Wilson and Dickinson in *J.A.M.A.* [*158*:261 (1955)], the compound apparently acts by permitting the hard fecal mass to be penetrated by water or by mineral oil so that it becomes effectively softened. No toxicity or irritation was evident during 12 years of use by the authors. There also was no evidence of interference with normal bowel function.

The compound is administered as a 1 per cent aqueous solution both orally and rectally as an enema. The bitter taste of the solution can be effectively disguised in the formula for infants or in fruit juices for children and adults. Dosage employed varied from 15 drops twice a day for infants to 2 ml. 3 times a day for adults. Enemas are frequently combined with oral therapy. Usually 30 to 60 ml. of mineral oil or sodium chlor-

—Continued on page 116a

Open the Flood Gates...

of the Biliary System with

CHOLAN h m b

The most comprehensive biliary therapy available

Formulated in a single tablet to provide SEDATION, synergistic with selective SPASMOLYSIS, plus potent HYDROCHOLERESIS

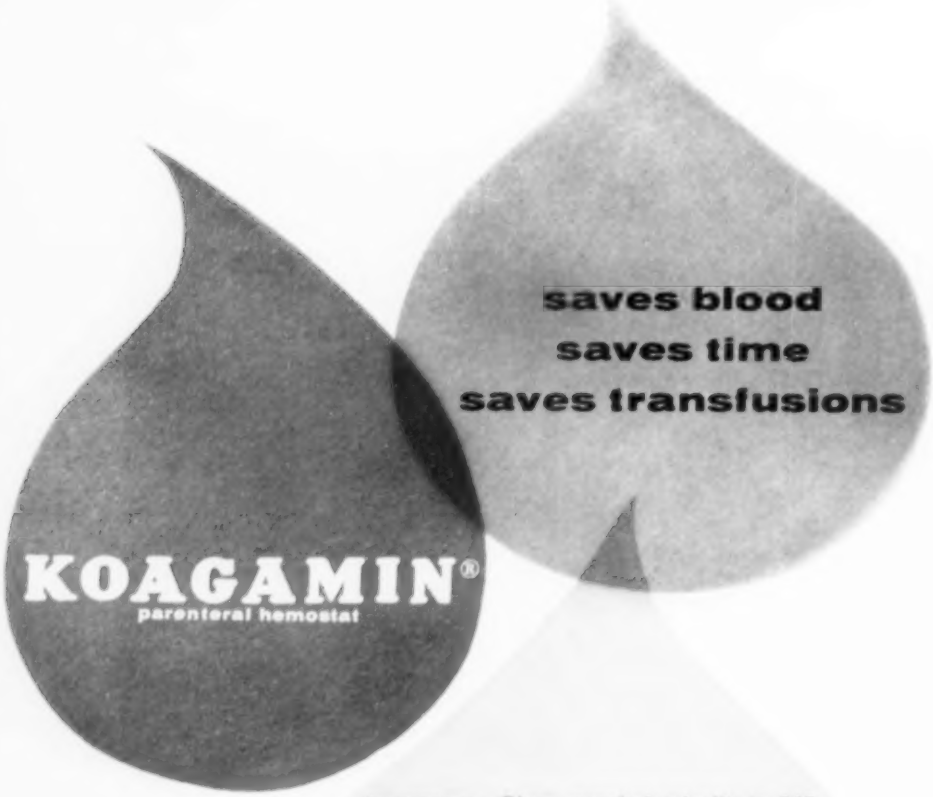
FORMULA:

Dehydrocholic acid	250.0 mg.
Homatropine methylbromide	2.5 mg.
Phenobarbital	8.0 mg.

Average dose is one tablet 3 times daily.

Liberal Sample mailed on request

MALTBIE LABORATORIES DIVISION • Wallace & Tiernan Inc. • Belleville 9, N. J.



in surgery—Given prophylactically in 567 surgical cases, a single injection of KOAGAMIN was found "...to reduce blood loss and to facilitate surgical procedures...often obviate[s] the use of transfusion...."*

in emergency—Acting directly on the clotting mechanism, KOAGAMIN arrests any capillary or venous bleeding in minutes—not hours, unlike vitamin K.

in inaccessible bleeding—By controlling hemorrhage of systemic origin, KOAGAMIN saves time and blood without the hazard of thrombosis or toxic reaction—no untoward effect ever reported.

*Joseph, M.: Am. J. Surg. *87*:905, 1954.

KOAGAMIN, an aqueous solution of oxalic and malonic acids for parenteral use, is supplied in 10-cc. diaphragm-stoppered vials.

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Rabellon®

COMPOUND OF BELLADONNA ALKALOIDS

time-tested treatment of parkinsonism

MAJOR ADVANTAGES: Provides three purified belladonna alkaloids for synergistic effect. Reduces rigidity and tremor. Improves mental outlook.

RABELLON steadies the palsied grip

For many years RABELLON has been effective in producing symptomatic relief of parkinsonism. A steadier hand, easier gait and better controlled speech are but a few of the benefits of continued therapy with RABELLON. Further, it is especially well-tolerated by elderly patients, and is recommended for patients sensitive to other antiparkinson agents.

RABELLON is a balanced combination of three alkaloids. Each RABELLON tablet contains hyoscyamine hydrobromide 0.4507 *mg.*, atropine sulfate 0.0372 *mg.* and scopolamine hydrobromide 0.0119 *mg.* Tablets are quarter-sected for convenient administration.

SHARP & DOHME

Philadelphia 1, Pa.
DIVISION OF MERCK & CO., INC.

—Continued from page 114s

ide solution was used as the vehicle for 5 ml. of 1 per cent dioctyl sodium sulfosuccinate solution.

Education and Sedation Found to Control Symptoms of Menopause

Recognizing that the severity of menopausal symptoms—hot flushes, irritability, nervousness, depression—bear a direct relation to and are very often caused, aggravated or prolonged by stress, anxiety, worry and tension, Dr. Harry S. Friedlander (*Postgraduate Medicine*, August 1955) treated 30 such patients over an eighteen month period with education and medical sedation.

The educational (or psychosomatic) phase of treatment consisted of explanation, encouragement and reassurance. The patient was told to regard her symptoms as largely normal and not something about which she need suffer fear, worry or anxiety. The entire process of the menopause was explained in simple terms. She was told that she might be "entering a period of greater contentment and accomplishment than ever before." Dr. Friedlander made it a point to uncover emotional factors which might be complicating the menopause, financial, marital, family discord, taking all the time necessary to create a state of mind essential for successful management of these patients.

Since education alone "seldom suffices to control symptoms immediately," Dr. Friedlander administered Seconesin, a combination of mephenesin and secobarbital, as a "safe, daytime sedative." In those patients who had difficulty in sleeping he prescribed Carbrital.

—Continued on page 120s

"Double-blind" Placebo-controlled Study Emphasizes Need for Stimulant Laxative in Chronic Constipation[1]

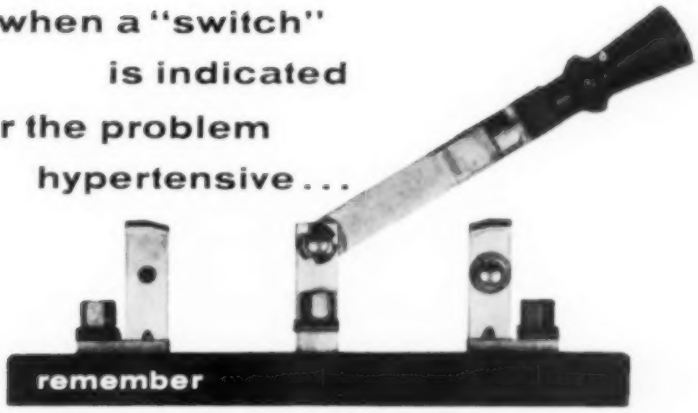
Caroid® and Bile Salts Tablets are deemed "particularly suited for use by the chronically constipated patient, especially the elderly, and by those postoperative patients in whom soft stools are particularly desirable."[2]

CAROID AND BILE SALTS Tablets are ideally suited for use in the management of constipation, particularly when associated with biliary stasis and impaired digestion.

American Ferment Company, Inc., 1450 Broadway, New York 18, N. Y.

1. Cass, L. J., and Frederik, W. S.: Ann. New York Acad. Sc. *58*:455 (July 15) 1954.
2. Shaftel, H. E.: J. Am. Geriatrics Soc. *1*:549 (Aug.) 1953.

when a "switch"
is indicated
for the problem
hypertensive . . .



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RUTOL

for safe,
round-the-clock
protection

RUTOL provides a three-way approach . . . *vasodilatation, protection against capillary hemorrhage, and sedation* . . . for management of:

- the "vascular accident-prone" patient whose capillary fragility complicates treatment
- the sclerotic patient who needs increased blood flow to the heart, brain, and kidneys
- the refractory patient who develops side effects during therapy
- the mild, labile hypertensive who does not need powerful drugs

Each RUTOL tablet contains:

Mannitol hexanitrate	16 mg.
Rutin	10 mg.
Phenobarbital	8 mg.

Dosage: One tablet four times daily after meals and at bedtime.

Supplied: Bottles of 100, 500, and 1,000 coated tablets.

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—Continued from page 118a

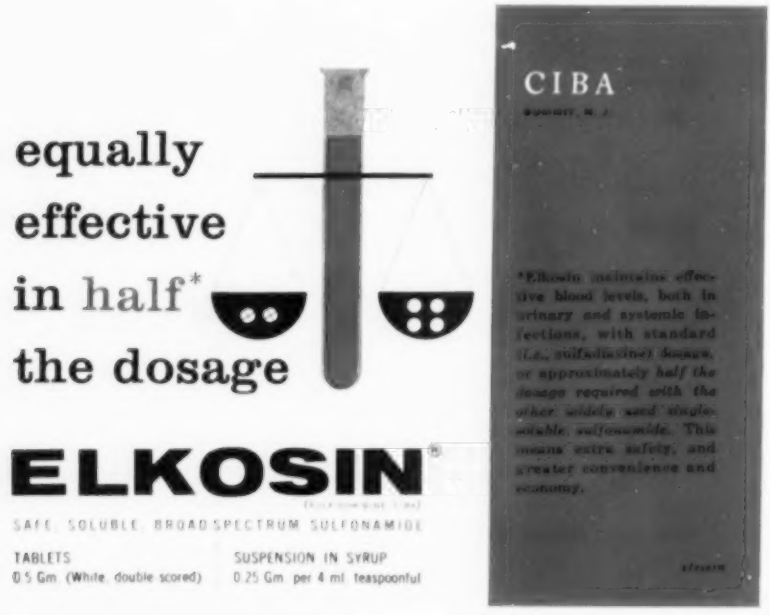
Infrequently, estrogens were used as a temporary measure. He believes, from his experiences, that only one patient in every 10, and only for a limited time, requires estrogenic hormones to control vasomotor symptoms since, generally speaking, the menopause is a transitional period. In his opinion estrogens tend to prolong this period.

The combination of mental reorientation and sedation with Seconesin and Carbrital, with occasional use of estrogens, successfully brought under control menopausal hot flushes, headaches, dizziness, nervousness, worry, anxiety, tension, fear, insomnia, irritability, the feeling of uselessnes. Seconesin was usually prescribed one tablet three times a day after meals. This team of relaxant mephenesin and sedative secobarbital was "found particularly useful for emotionally tense or anxious patients. It relaxes and calms without making patients sleepy or drowsy, there are no known contraindications, no serious or undesirable side effects, and patients do not develop a tolerance to it. In almost every case in which I have used Seconesin, subjective improvement has been sensed early; the patients experience a sense of well-being."

Hypertension of Acute Nephritis Treated with Hydralazine

Oral or intramuscular administration of hydralazine exerted a beneficial effect in the management of hypertension in acute nephritis patients. Hydralazine has a dual capacity, it reduces blood pres-

—Continued on page 122a



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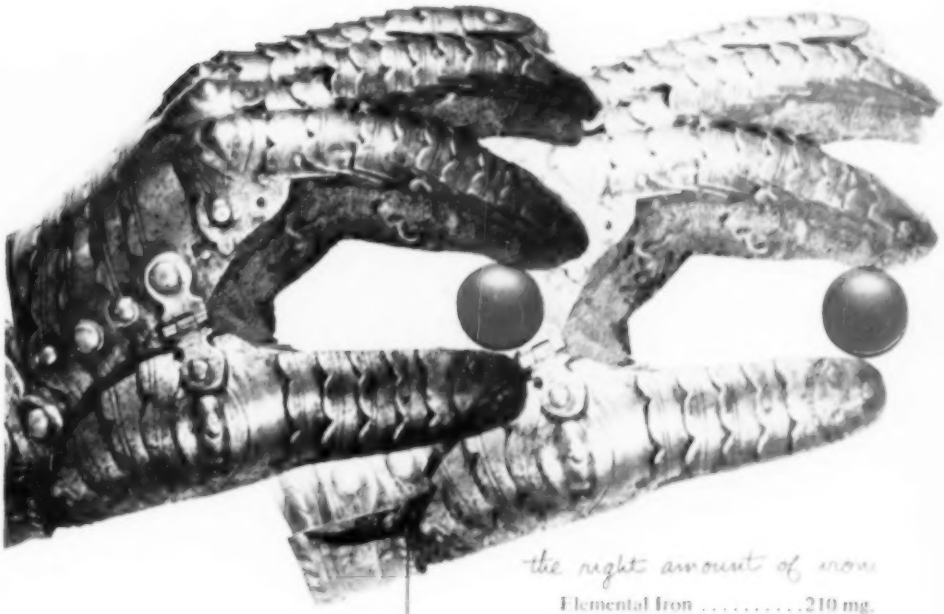

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Elemental Iron ..... 210 mg.
(as Ferrous Sulfate)

+

anti-pernicious anemia activity

BEVIDORAL® .. 1 U.S.P. Oral Unit
(Vitamin B_{12} with Intrinsic Factor Concentrate, Abbott)

+

essential nutritional factors

Folic Acid	2 mg.
Ascorbic Acid	150 mg.
Liver Fraction 2, N.F.	200 mg.
Thiamine Mononitrate	6 mg.
Riboflavin	6 mg.
Nicotinamide	30 mg.
Pyridoxine Hydrochloride	3 mg.
Pantothenic Acid	6 mg.

Abbott

complete 2-a day therapy for the anemias

—Continued from page 120a

sure and increases renal blood flow. This appeared to be ideal for the management of hypertension associated with acute glomerulonephritis, according to Tuttle, Etteldorf, Smith and Tharp in *Am. J. Dis. Children* [89:451(1955)].

There is, however, a temporary depression of renal function. In spite of this depression, the authors felt that the benefits, particularly in the presence of such complications as cardiac failure and encephalopathy, justify the use of hydralazine.

Ascorbic Acid and Bioflavonoids Aid in Habitual Abortion

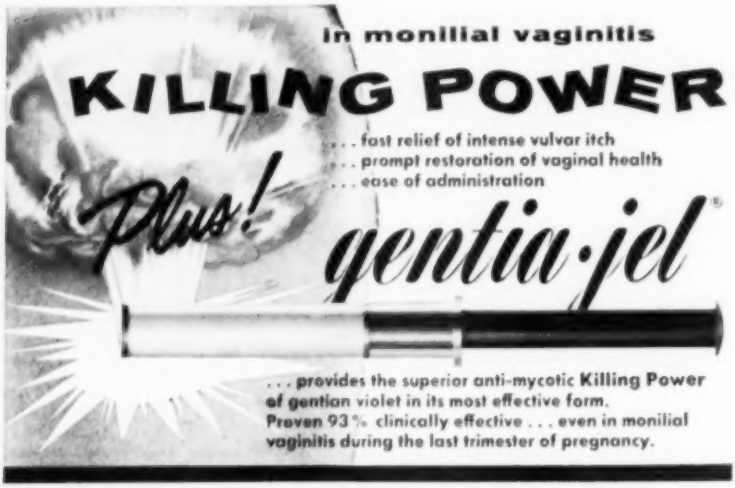
Speaking before the conference on bioflavonoids sponsored by the New York Academy of Sciences in New York City in February 1955, Dr. Robert Greenblatt, of the Medical College of Georgia, reported that capillary fragility had been observed in over 80 per cent of a group of women who were habitual aborters. This incidence was higher than normally expected.

When hesperidin and ascorbic acid were used to treat these patients, 4 of 7 patients who had had 3 to 8 successive abortions gave birth to live infants. Eleven of 13 with two previous abortions delivered live infants. Statistically, it would have been anticipated that without this therapy the live births would have been 1 and 8, respectively.

Psoriasis Responds to Rauwolfia Extract

High dosages of Rauwolfia extract were given to 14 patients for at least 2 months. Each of these patients had a

—Continued on page 124a



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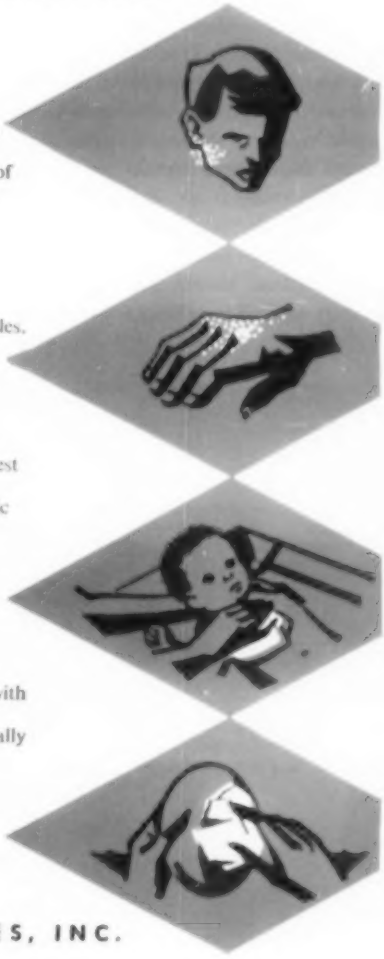


Acidolate

a non-lathering sulfated oil detergent, is the hypoallergenic skin cleanser of choice when a liquid emulsifying agent of low surface tension is required. It is an excellent cleansing agent in acne vulgaris, for removal of ointment and greases from the skin, hair or wounds, and as a shampoo for ringworm of the scalp.

Supplied: 8 fluid ounce and 1 gallon bottles.

Dermolate

"Milder than the mildest castile," a nonirritating detergent in cake form, is an ideal cleanser where even the mildest soap is poorly tolerated. It is ideally suited for routine use as a hypoallergenic skin cleanser; especially recommended for normal skin care of infants and young children.

Supplied: 4 ounce cakes.

Terjolate

a household cleanser designed for use with Acidolate and Dermolate, is neither irritating nor sensitizing—it is an unusually effective cleanser for all household purposes.

Supplied: 8 and 16 fluid ounce and 1 gallon bottles.

White

WHITE LABORATORIES, INC.

KENILWORTH, N. J.

—Continued from page 122a

severe degree of psoriasis. Nearly all of the patients showed a decrease or a disappearance of itching and a diminished redness and thickness of the plaques. Eight of the patients showed a more extensive improvement.

Genest, Adamkeiwicz, Robillard and Tremblay stated, in *Can. Med. A. J.* [72:490(1955)], that since Rauwolfia is known to cause a calming effect in psychologically disturbed patients, the results from these studies further give evidence to the truth of the theory that psychosomatic factors are a determining element in psoriasis.

The authors also found that reserpine therapy caused 4 patients who were normal in every way except that they were underweight, to gain from 7 to 12 pounds.

Ascorbic Acid and Hesperidin Reduce Complications of Anticoagulant Therapy

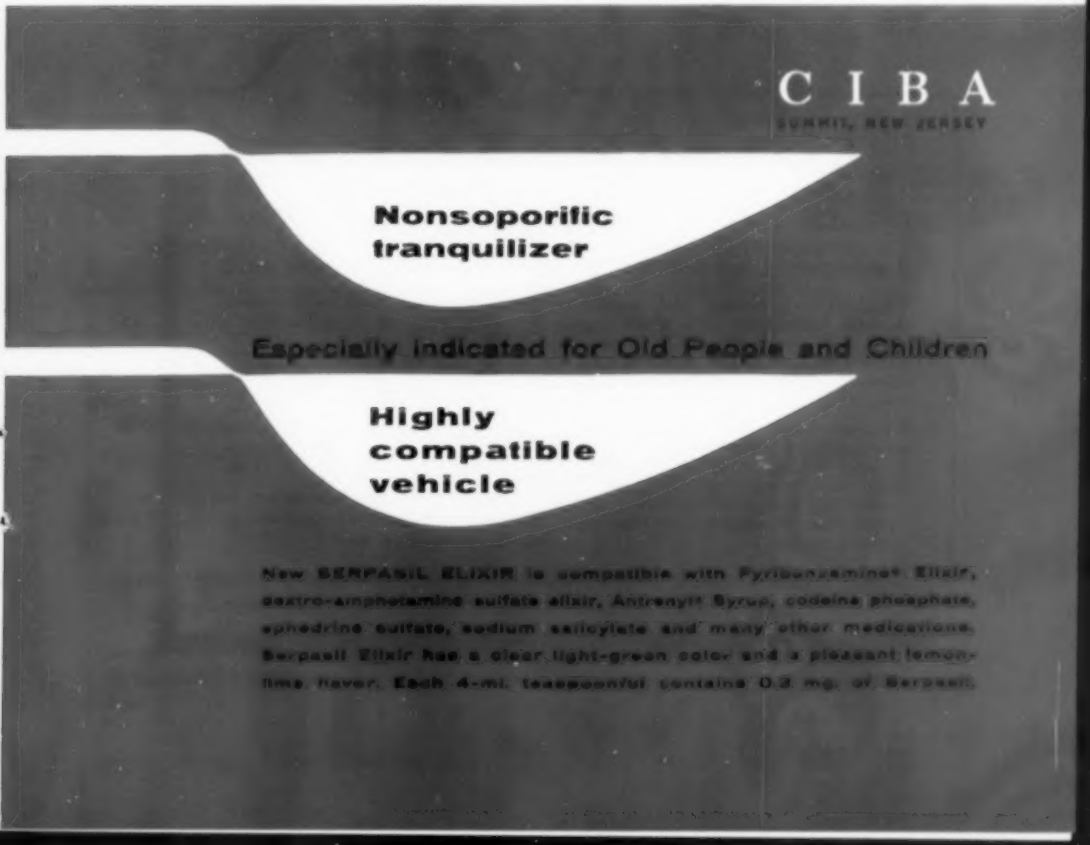
The administration of ascorbic acid and hesperidin has been found to help offset the capillary bleeding tendencies encountered in coumarin anticoagulant therapy, according to a report by Dr. Charles Brambel of Mercy Hospital, Baltimore, before the conference on bioflavonoids sponsored by the New York Academy of Sciences in February, 1955. The author suggested that the combined therapy acted by strengthening the capillaries. This therapy had been given to more than 2000 patients.

Serpasil®
(reserpine CIBA)
Elixir
Sedation without hypnosis

When given to patients in whom ecchymotic leakage had already begun, the ecchymotic areas cleared rapidly. Prior to this therapy, the purpuratic areas would have persisted for a much longer period and anticoagulant therapy would probably have had to have been discontinued. When ascorbic acid-hesperidin therapy was begun at the time anticoagulant therapy was begun in a group of 200 patients, hemorrhage complications were prevented. Normally 5 per cent would have been expected to have capillary bleeding.

Hexamethonium, Hydralazine and Rauwolfia Serpentina Therapy in Hypertension

In order to evaluate the effects of certain drugs on hypertension, Meyer Markovitz and his co-workers, *American Journal of the Medical Sciences*, [229: 436 (1955)] established a clinic for hypertensive vascular disease. The drugs studied were hexamethonium, hydralazine and Rauwolfia serpentina. Patients selected were considered in four groups according to the degree and severity of the disease: (1) Patients in whom the disease was mild; (2) Patients in a more severe stage of the disease; (3) Patients with "malignant" hypertension; (4) Patients having previously undergone sympathectomy. In an evaluation of therapy for hypertensive vascular disease comparing similarly affected groups as well as determining an index of therapeutic effect present major problems. The use of blood pressure for the latter purpose has decided lim-



itations. From observations made, Rauwolfia serpentina seemed to be best for ambulatory patients with hypertensive vascular disease. Hexamethonium should be used only for patients in a severe stage of the disease. Recurrent syncopal episodes are a definite possibility especially in patients having had sympathectomy. Hydralazine or Rauwolfia serpentina or both when given with hexamethonium produce greater reductions in blood pressure, reduce the required amount of hexamethonium, and decrease untoward side-effects.

Tyzine as a Topical Vasoconstrictor

A sympathomimetic agent, Tyzine, was used in a 0.1-per cent aqueous solution as a nasal spray or as nose drops in treating a group of patients with nasal blocking from various causes: Postnasal drip was included. The topical application of pressor agents such as Tyzine produces local constriction of the small blood vessels thus relieving the inflammatory hyperemia and edema of nasal congestion. The author, H. C. Menger, in reporting the result of his investigations in the *New York State Journal of Medicine* [55:812 (1955)] is of the opinion that the spray reaches affected mucous membranes more effectively than drops. Instillations of Tyzine averaged four times daily; the vasoconstrictive response appeared immediately. In most instances, bedtime instillations gave relief throughout the night. In the group studied, 92 per cent of the patients received marked benefit.

—Continued on page 128a

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FOLBESYN*

Vitamins *Lederle*

A well-balanced, high-potency vitamin formula containing B-Complex and C

FOLBESYN provides B-Complex factors (including folic acid and B_{12}) and ascorbic acid in a well balanced formula. It does not contain excessive amounts of any one factor.

FOLBESYN Parenteral may be administered intramuscularly, or it may be added to various hospital intravenous solutions. It is useful for preoperative and postoperative treatment and during convalescence.

Dosage: 2 cc. daily. Each 2cc. provides:

Thiamine HCl (B_1)	10 mg.
Sodium Pantothenate	10 mg.
Niacinamide	50 mg.
Riboflavin (B_2)	10 mg.
Pyridoxine HCl (B_6)	5 mg.
Ascorbic Acid (C)	300 mg.
Vitamin B_{12}	15 micrograms
Folic Acid	3 mg.

FOLBESYN is also available in tablet form, ideal for supplementing the parenteral dose.

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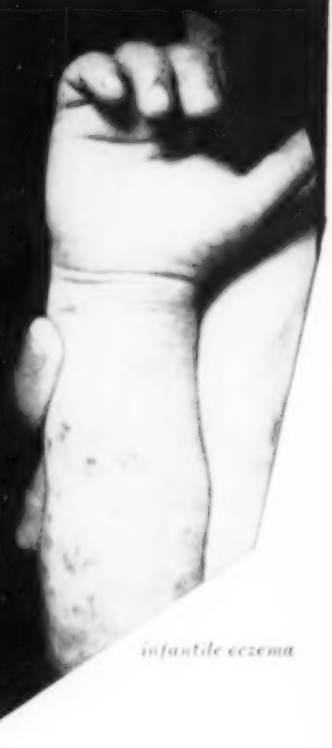
combined corticosteroid-antibiotic therapy for dermatologic conditions

. . . including poison ivy and sunburn



infantile eczema

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Ointment
Lotion

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the anti-inflammatory, anti-pruritic action* of FLORINEF —much more potent than that of topical hydrocortisone

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the prophylactic action* of SPECTROCIN—effective against many gram-positive and gram-negative organisms

*". . . secondary infection with pustulation often follow scratching which is induced by the intense itching." Nelson, W. E.: Textbook of Pediatrics, ed. 5, Philadelphia, W. B. Saunders Company, 1950, p. 1516.

Supply: Florinef-S Lotion, 0.05 and 0.1 per cent, in 15 ml. plastic squeeze bottles. Florinef-S Ointment, 0.1 per cent, in 5 gram and 20 gram collapsible tubes.

Also available: Florinef Lotion, 0.05, 0.1 and 0.2 per cent, in 15 ml. plastic squeeze bottles. Florinef Ointment, 0.1 and 0.2 per cent, in 5 gram and 20 gram collapsible tubes.

"FLORINEF-S", "FLORINEF" AND "SPECTROCIN" ARE SQUIBB TRADEMARKS

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METICORTEN
PREDNISONE (metacortandracin)
more potent than cortisone or hydrocortisone • devoid of major undesirable side effects
METICORTEN,* brand of prednisone.
*T.M.
SCHERING
Schering

MODERN THERAPEUTICS

—Continued from page 126a

only 0.5 per cent were unaffected by the treatment, and the remainder obtained fair results. It is noteworthy that even when Tyzine was used continuously for as long as two weeks, no untoward side-effects occurred.

Therapeutic Agents in Rheumatic Carditis

Observations were made on a group of young men at the Warren Air Force Base Hospital to ascertain the effects of certain drugs on valvular heart disease as evidenced by the presence of murmurs 14 months after the beginning of therapy. Prophylaxis against streptococcal infections was maintained throughout the period. The drugs compared were acetylsalicylic acid, cortisone and corticotropin. It was discovered that no one drug exhibited marked advantages over the others in the treatment of the

—Continued on page 130a

MEDICAL TEASERS

Solution to puzzle on page 41a

F	A	M	A	■	T	U	M	O	R	■	A	S	P	S
A	D	A	M	■	A	T	A	X	Y	■	W	A	A	C
U	D	O	■	A	L	A	■	Y	O	N	■	D	R	U
N	I	■	B	B	C	■	C	■	T	H	E	■	T	T
A	S	S	A	Y	■	M	O	A	■	C	A	C	H	E
L	O	I	N	■	P	A	L	N	P	■	R	U	E	S
■	N	G	■	B	O	L	L	A	R	D	■	T	N	■
O	S	■	T	R	I	F	O	L	I	U	M	■	O	S
■	D	Y	■	A	N	O	D	Y	N	E	■	M	G	■
B	I	O	S	■	T	R	I	S	T	■	D	I	E	S
A	S	U	R	S	■	M	A	T	■	M	A	G	N	A
L	E	■	L	A	C	■	N	■	R	A	M	■	E	C
S	A	C	■	L	O	X	■	E	S	T	■	A	S	H
A	S	C	I	■	D	E	R	M	A	■	B	R	I	E
M	E	S	O	■	E	N	N	U	I	■	L	A	S	T

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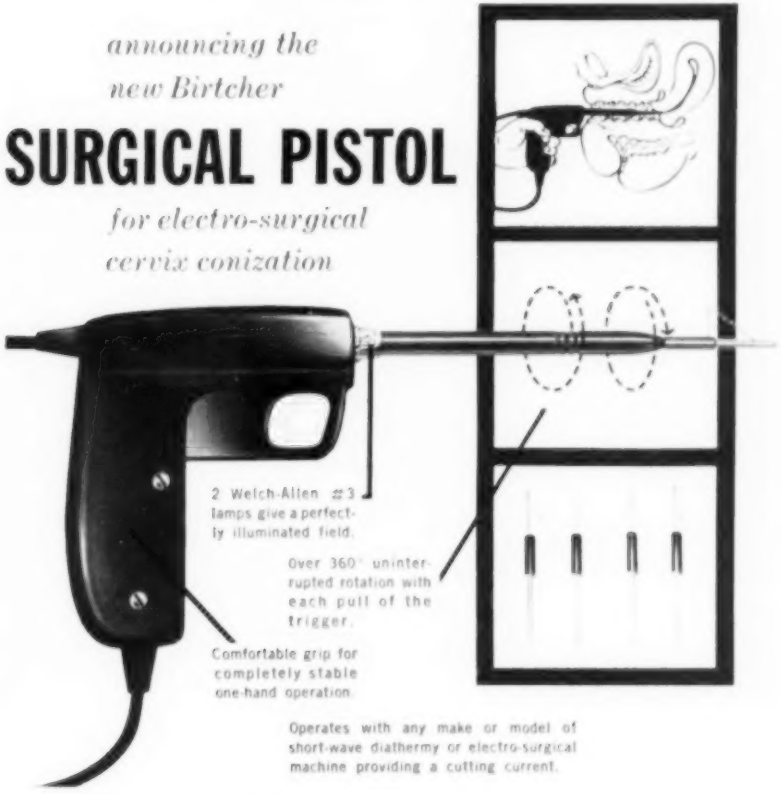

The Birtcher Surgical Pistol offers surgical accuracy, less operating time, less strain on surgeon and patient. Since the Pistol is operated with one hand, the other is free for other instrumentation. Because of the delicate touch of the instrument, the surgeon retains his surgical "feel." The greater stability and control results in smooth, uniform excisions with no ragged tissue as a possible site for post-operative infection. Two built-in lights give a perfectly illuminated field.

No. 756 Birtcher Surgical Pistol Set complete with 2 lamps, 4 Hawkins Electrodes and connecting cord is priced at **$65.00.** When ordering, specify make and model of electro-surgical unit or short wave diathermy.

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CITY _____ ZONE _____ STATE _____

—Continued from page 128

acute manifestations of rheumatic fever. In the study conducted by Capt. B. L. Stolzer (MC) U.S.A.F. and his associates *Archives of Internal Medicine* [95:677 (1955)], it appeared, however, that while some patients under treatment with each of the drugs mentioned, developed murmurs during the 14-month period, the fewest significant murmurs occurred in the cortisone-treated group. Most of the murmurs heard were of the apical systolic type; cortisone appeared to prevent the appearance of these murmurs and to cause the disappearance of those existing to a greater degree than did the other two drugs. Its seemingly favorable effect suggests further investigation.

Drug Therapy of Hypertension

In treating a disease such as hypertension, the therapeutic agent should be evaluated only after a lengthy follow-up period. The authors, Moser and Mattingly, writing in *Postgraduate Medicine* [17:351 (1955)], believe that an appraisal of certain of the newer drugs is now feasible, and give the results of their observations. *Reserpine*, though offering no striking results, was somewhat effective in early nonprogressive hypertension, but proved of more value when used in combination with more potent agents whose dosage could thereby be decreased. Side-effects are minimal. *Apresoline*, used parenterally,

—Continued on page 132

ATHLETE'S FOOT

needn't be a vicious circle..

...if you use

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You *think* you've got the case licked... when *back comes the patient for more treatment!* Either it's dormant fungi, springing back to life . . . or overtreatment dermatitis, the result of an overpowering caustic . . .

Now turn the case over to OCTOFEN Liquid and Powder . . . for *definitive* results!

OCTOFEN being truly *fungicidal* . . . not weakly *fungistatic* . . . is out to *kill* fungi . . . not render them somnolent. And *kill* them OCTOFEN does! Not just superficially – but at sub-layer levels. OCTOFEN's clinically proven formula including 8-hydroxyquinoline benzoate does this . . . penetrating even exudate and debris. Highly potent, but low in concentration, OCTOFEN is gentle, thus minimizing the risk of excruciating overtreatment dermatitis. For heartening results, backed by 90% effectiveness in clinical tests, rely on OCTOFEN.

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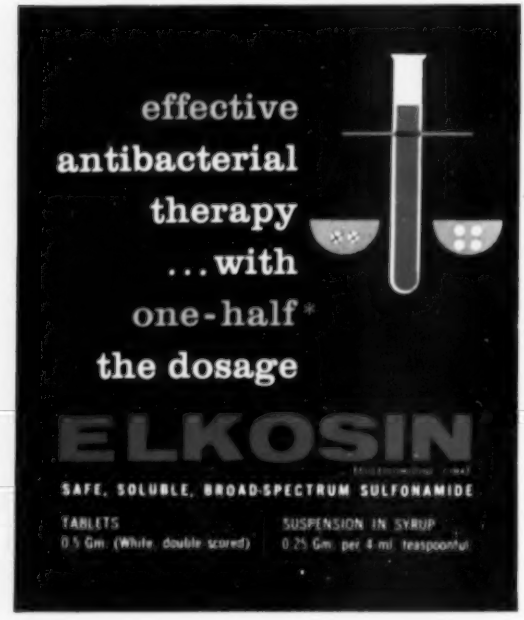
—Continued from page 130a

has a potent hypotensive effect, and is valuable for treating the toxemia of pregnancy. Its application to Grade I hypertension does not appear warranted, but it is most effective in the severe grades, especially when used in combination. If given alone, the average daily dose is 400 to 600 mg.; when used with hexamethonium or Rauwolfia, the daily amount used is 300 to 400 mg. Side effects though numerous are seldom severe. *Hexamethonium* and *Ansolysen* are the most potent hypotensive agents available for use in severe degrees of hypertension. Gratifying results are possible if necessary caution is observed in their administration. Symptoms and signs of side-effects should receive prompt attention. Best results are achieved with combined therapy.

Phosphoramide Chemotherapy to Control Neoplastic Effusion

The intracavitary injection of phosphoramide agents was used on a group of so-called hopeless cancer patients to observe the effect of the agent on serous effusion. The prepared solution was administered into the pleural, abdominal or pericardial cavity after withdrawal of the fluid. According to J. C. Bateman and her co-workers by whom the observations were reported in the *Archives of Internal Medicine* [95:713 (1955)], the best results were obtained in patients with mammary and ovarian carcinomata, the control of pleural effusion having lasted from one to nine

—Continued on page 134a



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*Elkosin maintains effective blood levels, both in urinary *and* systemic infections, with standard (i.e., sulfadiazine) dosage, or approximately *half the dosage required with the other widely used soluble sulfonamide.* This means extra safety, and greater convenience and economy.

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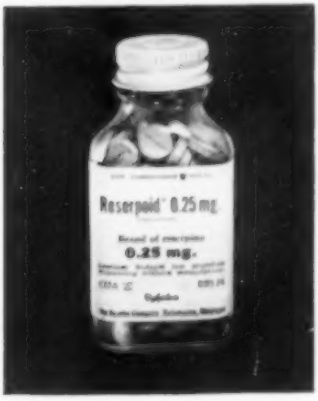
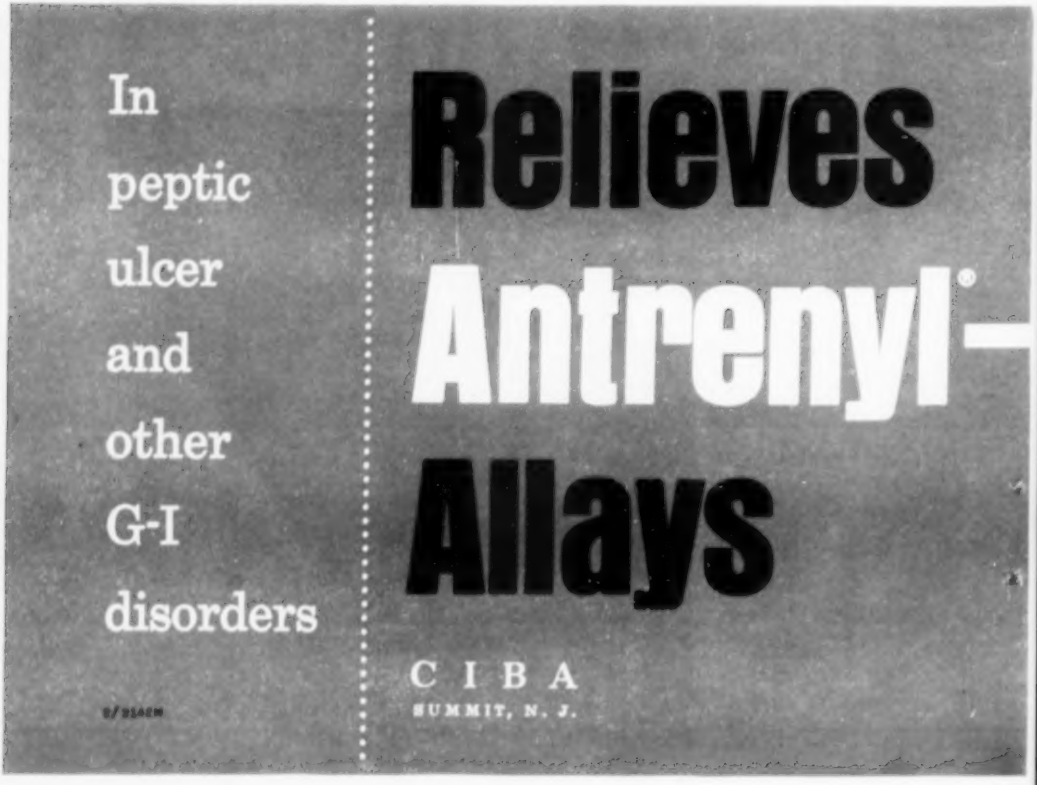


Continued from page 62a

months. These patients were enabled to resume partial or full activity because fluid reaccumulation had been controlled. Intracavitary administration of the phosphoramides is easily accomplished, and an absence of side-effects permits their use without hospitalization of the patient. Also, nontumor tissue is apparently unaffected by this therapy.

Dicumarol and Heparin in the Treatment of Myocardial Infarction

Although no definite conclusion is accepted as to the value of anticoagulants in the treatment of myocardial infarction, the author, Solomon Garb, of the Cornell University Medical College, *American Journal of the Medical Sciences* [229:534 (1955)] discusses pertinent factors pertaining to heparin and dicumarol when used in this connection. Heparin is an anticoagulant, but little is known about its effects in myocardial infarction. For the most part, heparin has been used for a brief time until the desired effect of dicumarol on the prothrombin time has developed. A period of 24 to 48 hours elapses before the effects of dicumarol are manifested by a significantly lowered blood prothrombin content. A study was conducted using "treated" and "control" patients. Among the



patients receiving dicumarol there was a significant decrease in the number who developed thromboembolic complications. Also, in the "treated" group the percentage of fatalities showed a definite decline. While opinions differ on the dangerous reactions from dicumarol, many believe that with necessary precautions, regulated dosage and careful attention to prothrombin levels, the toxicity is not great.

Chlorpromazine Therapy and Regurgitation Type of Jaundice

There has been very slight indication of hepatic toxicity following the administration of chlorpromazine even in the presence of known liver disease, a fact which prompted the authors, Lemire and Mitchell, to report the histories of three cases of regurgitation jaundice which developed during the administration of this drug *Archives of Internal Medicine* [95:340 (1955)]. One patient received a total of 3360 mg. of chlorpromazine, with the highest daily dosage 200 mg.; jaundice appeared after 23 days. A second patient received a total of 1350 mg. of the drug, the highest daily amount being 100 mg.; jaundice appeared after 15 days. The third patient's total dosage was 1520 mg., the highest daily amount was 50 mg., and the appearance of jaundice occurred after 31 days. In each instance, the only systemic manifestation was pruritus. Surgical jaundice could

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in the anemias... RONCOVITE *is...*

Therapeutically Unique

"...cobalt is indicated in all cases in which the slowly regenerating marrow requires a more forceful hematopoietic stimulus than is given by physiologic activators or a therapeutically elevated iron level."

—Wolff, H.: Med. Monatschr. *5*:239 (April) 1951.

"These studies show that oral cobalt therapy can stimulate erythropoiesis..."

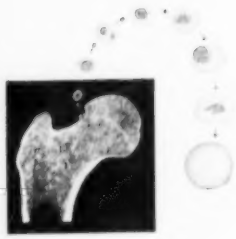
—Gardner, F. H.: J. Lab. & Clin. Med. *41*:56 (Jan.) 1953.

"Cobalt seems to stimulate...the bone marrow which undergoes progressive hyperplasia of all cellular elements with a consequent discharge of erythrocytes into the circulation."

—Kato, K.: J. Pediat. *11*:385 (Sept.) 1937.

"In our series of cases, cobalt proved to be a powerful stimulant to erythropoiesis..."

—Rohn, R. J.; Bond, W. H., and Klotz, L. J.: J. Indiana State Med. Assn. *46*:1253 (Dec.) 1953.



"Hematopoietic responses to therapy with cobaltous chloride, which were observed in each patient, indicate that cobaltous chloride produced an active stimulus to erythropoiesis..."

—Robinson, J. C., et al.: New England J. M. *240*:749 (May) 1949.

Roncovite has introduced a wholly new concept in the prevention and treatment of anemia. It is based on the unique hemopoietic stimulation produced only by cobalt.

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IN INFANCY—"The therapy used by us [Roncovite] was approximately equivalent in results to the transfusion of 1½ pints of blood weekly in adults."

—Rohn, R. J.; Bond, W. H., and Klotz, L. J.: J. Indiana State Med. Assn. *46*:1253 (Dec.) 1953.

"Cobalt appears to be of value in the prevention of the early anemia of premature infants, and if iron is administered simultaneously the risk of an iron deficiency anemia developing from the fourth month onwards is considerably reduced."

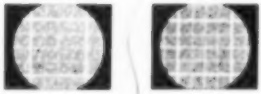
—Coles, B. L., and James, U.: Archives of Disease in Childhood, *29*:85 (April) 1954.

As compared with controls, 16 premature infants receiving Roncovite Drops showed "significantly greater values in the mean hemoglobin and hematocrit levels..."

—Quilligan, J. J., Jr.: Texas St. J. Med. *50*:294 (May) 1954.

IN PREGNANCY—"...57 of the 58 patients (98.2 per cent) maintained or improved their hemoglobin [with Roncovite]..."

—Holly, R. G.: Obstet. & Gynecol., *5*:562 (April) 1955.



IN CHRONIC LOW-GRADE INFECTIONS—"Cobalt appears to be a valuable drug in the treatment of anemias secondary to chronic diseases."

—Weinsaft, P. P., and Bernstein, L. H. T.: Amer. J. Med. Sc., Vol. 229, (Sept.) 1955.

"In all patients (chronic suppurative infection) a reticulocytosis was observed within 6 days. This was followed by increases in red-cell counts, in hemoglobin values, in blood volume and in total circulating hemoglobin."

—Robinson, J. C., et al.: New England J. M. *240*:749 (May) 1949.

Safe Medication

IN INFANCY—"There were no toxic effects in any case."

—Coles, B. L.: Archives of Disease in Childhood, *30*:150 (April) 1955.

"None of them [infants] showed harmful effects despite the large doses."

—Quilligan, J. J., Jr.: Texas St. J. Med. *50*:294 (May) 1954.

IN PREGNANCY—"No toxic manifestations associated with its use have been observed."

—Holly, R. G.: Obstet. & Gynecol. *5*:562 (April) 1955.

IN CHRONIC LOW-GRADE INFECTIONS—"With 60 mg. (cobalt chloride) a day by mouth after meals neither ourselves nor our patients experienced untoward symptoms."

—Robinson, J. C., et al.: New England J. M. *240*:749 (May) 1949.

"In our hands, cobalt appeared to be a useful and valuable drug, well tolerated and devoid of undue toxicity."

—Weinsaft, P. P., and Bernstein, L. H. T.: Amer. J. Med. Sc., Vol. 229, (Sept.) 1955.

AND . . . Thorough investigation has again verified the safety and lack of toxicity of Roncovite. Please refer to the four articles in the August 13, 1955 issue of the J.A.M.A. (Volume 158, No. 15) which fully document this convincing evidence.

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Cobalt chloride	15 mg.
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Each 0.6 cc. (10 drops) provides:

Cobalt chloride (0.9 mg. cobalt)	40 mg.
Ferrous sulfate	75 mg.

Bottles of 15 cc. with calibrated dropper

DOSAGE:

One tablet after each meal and at bedtime. Children 1 year or over, 0.6 cc. (10 drops); infants less than 1 year, 0.3 cc. (5 drops) once daily diluted with water, milk, fruit or vegetable juice.

—Continued from page 136

not be excluded, and all three patients underwent surgery; but without findings to account for the condition. The three patients showed a progressive decrease in jaundice, and were anicteric 117, 108 and 55 days after its onset.

Elorine Sulfate and Co-Elorine Clinically Evaluated

Elorine sulfate and Co-Elorine were investigated as to their efficacy in the treatment of gastrointestinal conditions and their effect on gastric secretion. Of the 167 patients with various gastrointestinal disorders studied, 116 had peptic ulcers. Twelve of these patients could not be followed satisfactorily. Of the remainder, 74 per cent were classed as successfully treated. I. R. Schwartz and his co-workers, *American Journal of Gastroenterology* [23:461 (1955)], are of the opinion that the percentage would have been higher if a larger dosage than that of 50 mg. four times daily had been used. Doses of 75 or 100 mg. four times daily could be used safely, while the 50-mg. dose would be adequate for maintenance. Patients in the other groups treated showed substantially the same percentage of beneficial results, but the numbers were too small to be statistically significant. Gastric secretion studies showed diminu-

tion of volume and free acid when the dose of Eforine sulfate was 100 mg. or more. Side-effects were moderate; thirty-four per cent of the patients were free of reactions, while the others complained mostly of dryness of the mouth, blurring of vision, and constipation.

Trilene in General Practice

Trilene, or trichlorethylene, is a stable liquid at ordinary temperatures, and non-inflammable except when mixed with high concentrations of oxygen. Above 125 degrees F., it decomposes into phosgene and hydrochloric acid. It is colored blue to distinguish it from chloroform to which it is similar, and comparable in potency. The inhaler for its use as an analgesic is simple and compact, and readily available for use in office or clinic. However, any excess fluid on the inhaler or condensations on the mask should be avoided to prevent possible burns or blisters of the skin. The author, A. M. Phillips, in an article appearing in *The Mississippi Doctor* [33:15 (1955)] stresses the differences involved in using trilene as an analgesic or as an anesthetic. As an analgesic, trilene may be administered without specially trained personnel. Both induction and recovery are rapid, and neither fasting nor pre-medication is necessary. Trilene is being used with increasing frequency for minor surgi-

Broad Antibacterial, Antifungal Activity in External and Chronic Middle Ear Infections

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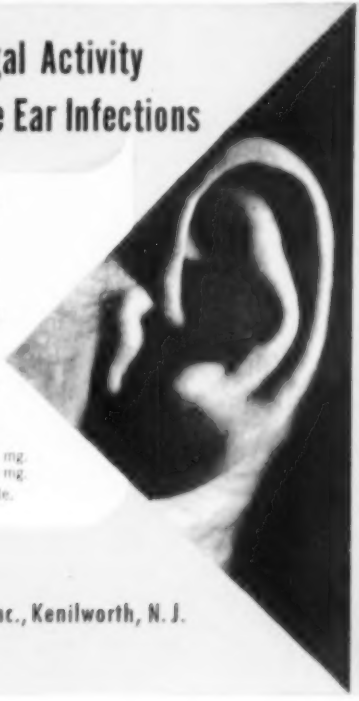

...combined neomycin-sodium propionate therapy
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...pH conforms to slightly acid condition of the normal external ear

Each cc. contains:
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...in an autogenously sterile hydroalcoholic glycerin vehicle.

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cal and dental procedures and in obstetrics. In deliveries, the patient may be instructed in the self-administration of trilene, but an attendant should be present at all times to remove the mask between contractions or in the event of loss of consciousness by the patient. If analgesic concentrations of trilene are exceeded, trained personnel and anesthesia equipment should be available. It has been pointed out that the use of this agent as an anesthetic is pushing it beyond its intended use. Also, pre-existing cardiovascular or hepatic disease are definite contraindications to its employment.

Office Treatment of Hypertension with Cryptenamine and Reserpine

A group of 11 ambulatory clinic patients were given cryptenamine, an alkaloid prepared from veratrum viride, later combined with reserpine, an alkaloid derived from rauwolfia. The average daily dose of cryptenamine ranged from 10 to 16 milligrams, and of reserpine, from .01 to 1.0 milligrams. Burton M. Cohen, writing in the *Journal of the Medical Society of New Jersey* [52:342 (1955)], has followed up a previous report on cryptenamine in which a definite decrement in systolic, diastolic and mean blood pressure was recorded.

The addition of reserpine was associated with the enhancement of the hypotensive response. Side-effects, noted by more than half of the patients treated with cryptenamine alone, were largely eliminated when the two drugs were combined. The headache was the symptom most effectively relieved.

CIBA
SUMMIT, N. J.

*Elkosin maintains effective blood levels, both in urinary and systemic infections, with standard (i.e., sulfadiazine) dosage, or approximately half the dosage required with the other widely used single-soluble sulfonamide. This means extra safety, and greater convenience and economy.

WHENEVER RAUWOLFIA SERPENTINA OR CHLORPROMAZINE CAUSES NASAL CONGESTION

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NOT "JUST ANOTHER" DECONGESTANT!

Make it a habit to prescribe Rhinalgan Nasal Spray to prevent nasal congestion whenever you prescribe chlorpromazine or rauwolfia serpentina preparations. *J. N. Y. Phys., 31:11, 1950.*

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NEWS AND NOTES

Brainwashing May Produce Problems in Future

Chinese Communist brainwashing may play a part in producing future psychiatric symptoms in returnees from Korean POW camps, two St. Louis physicians said today.

They also suggested that because of the intensity of the conflict between ideas absorbed in the camps and American thinking, there may be more psychiatric problems in Korean returnees than in a comparable group from German and Japanese POW camps of World War II.

The desire to avoid just such a conflict may have been the reason some prisoners chose to remain in China, they said.

Drs. Peter S. Santucci and George Winokur, from the department of neuropsychiatry of Washington University School of Medicine, outlined the brainwashing technique and the conflicts it can produce in a recent issue of *Archives of Neurology and Psychiatry*.

"Brainwashing is not merely a method of indoctrination," they said. It is a process which can produce abnormal human behavior through the development of internal conflicts and their accompanying anxiety and confusion.

METIC

PREDNISONE (metacortandracin)

more potent than cortisone or hydrocortisone · devoid of major undesirable side effects

In brainwashing, prisoners were forced to do certain things, such as sing Communist songs and write pro-Communist statements. When they did not rebel, they were rewarded, usually with extra food. Thus the desirability of this behavior was "reinforced," and the action was more likely to be repeated.

However, if the man did not believe in his statements and activities, internal conflict "inevitably" would result.

A prisoner could solve the conflict in one of three ways. He could outwit his captors by lying. He could refuse to do the bidding of his captors, which would result only in short-lived punishment. Or he could start thinking in favor of his captors, which would result in more rewards and more reinforcement of this behavior.

If he chose the third way, another conflict could occur after his return home, when he would begin to compare American concepts with those ideas absorbed in the prison camp.

The doctors used as an example the case of a 25-year-old Army sergeant of poor economic and educational background, who became mentally ill on his return home from a POW camp.

While a prisoner, he had been forced to attend lectures, where Communist and anti-American propaganda was repeated over and over. Later he was picked for several special duties and eventually sent to an advanced indoctrination school.

Although he probably did not accept the Communist ideas at first, he was rewarded for his activities. In time he

(Continued on page 142)

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METICORTEN,* brand of prednisone.

*T.M.

DESPITE PRESENCE OF MUCINOUS MATERIAL AND BLOOD SERUM

ALL TRICHOMONADS

ARE DESTROYED IN 30 SECONDS![1]

The new trichomonacide, Vagisec* jelly and liquid, clears up even stubborn clinical cases of vaginal trichomoniasis. Used with the Davis technic, it penetrates to hidden trichomonads—ends treatment failure and flare-ups.

Vagisec liquid penetrates to trichomonads buried among the vaginal rugae and imbedded in mucus and desquamated cells.

Trichomonads explode within seconds. "Motion pictures taken through a phase-contrast microscope at 24 frames per second, show that most trichomonads are destroyed within ten seconds after contact with a 1:250 solution. . . . Even in the presence of blood serum and mucinous material all are destroyed within 30 seconds."[1]

Explosion succeeds. ". . . over 90% of apparent cures have been obtained . . ."[1] with Vagisec liquid. This preparation "has proved in vitro to be over ten times as effective in killing T. vaginalis, when compared with any of the douche powders available through the drug trade."[1] Vagisec jelly stays in the vagina to destroy trichomonads at night.

Why they explode. Three chemical components of Vagisec liquid attack the trichomonad synergistically. A chelating agent complexes and takes away the calcium of the calcium proteinate. A wetting agent removes lipid materials. A detergent denatures the protein. The parasite imbibes water, swells up and explodes.

The Davis technic.† Dr. Carl Henry Davis, well-known gynecologist and author, and C. B. Grand, research physiologist, introduced this new trichomonacide as "Carlendacide." Over one hundred leaders in obstetrics and gynecology tested it clinically and found it a remarkably fast-acting, effective therapy. Doctor Davis recommends a combination of 1) Vagisec liquid in office treatment; 2) home treatment with Vagisec jelly at night and 3) douche with Vagisec liquid in the morning. "A few women have infected cervical, vestibular or urethral glands and require other types of treatment . . ."[1]

Vagisec jelly and liquid are non-toxic and non-irritating. In a recent collected study only about one per cent of women showed evidence of allergy to Vagisec liquid.[1]

Office Treatment. Expose vagina with speculum. Wipe walls dry with cotton sponges and wash thoroughly for about three minutes with a 1:250 dilution of Vagisec liquid. Remove excess fluid with cotton sponges. Dr. Davis recommends six office treatments.

Home Treatment. Patient inserts Vagisec jelly each night and douches with Vagisec liquid (2 teaspoonfuls in 2 quarts of warm water) each morning except on office treatment days. Continued douching two or three times a week helps to prevent re-infection. Pregnant women should have office treatments only.

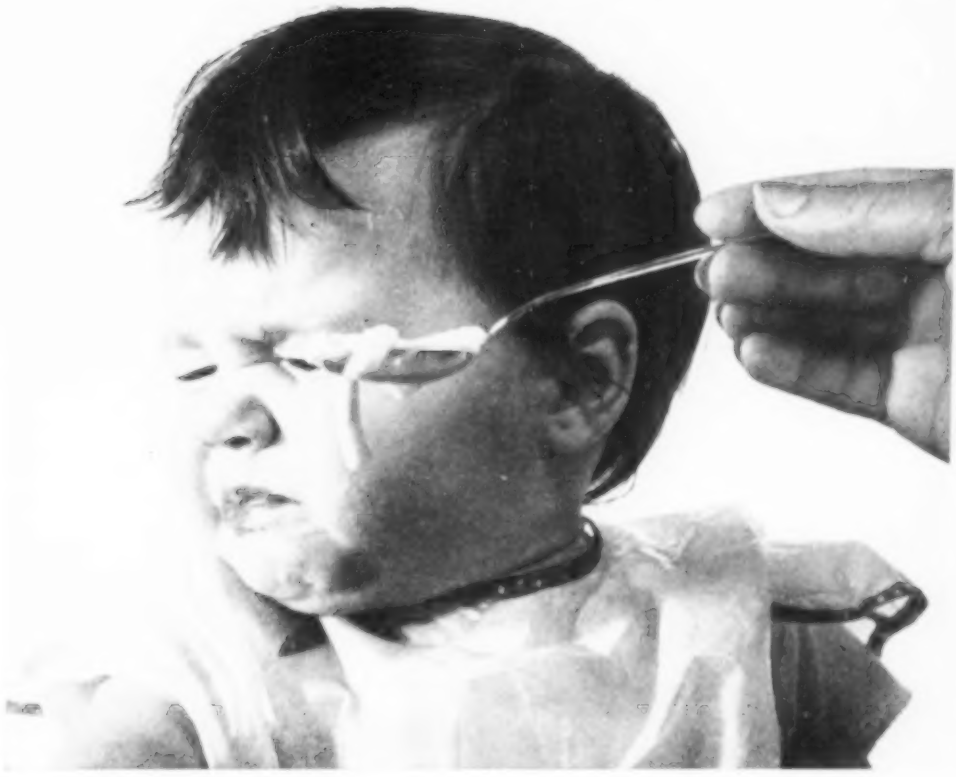
Summary. The unique synergistic action of Vagisec liquid explodes both hidden and surface vaginal trichomonads. This therapy has a high apparent cure rate and results in fewer flare-ups. Vagisec jelly and liquid are non-toxic and non-irritating, and leave no messy discharge or staining.

1. Davis, C. H.: West. J. Surg. 63:51 (Feb.) 1955.

*VAGISEC is the trade mark of JULIUS SCHMID, INC. †Pat. Apl. for

JULIUS SCHMID, INC., *gynecological division*
423 West 55th Street, New York 19, N. Y.

Active ingredients: Polyoxyethylene lauryl ether, Sodium alkylene diamine tetra acetate, Sodium dioctyl sulfosuccinate, in addition vaginally acting complex boric acid. Acidity 3.5 by weight



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The Complete Pediatric Nutritive Supplement

the first pediatric dietary formulation to provide adequate quantities of L-lysine for optimal growth and for the stimulation of normal appetite—

PLUS *all* essential vitamins in excess of dietary allowances,

PLUS essential iron and calcium.

2 measures (2.3 Gm.) of Lactofort supply:

L-lysine (from L-lysine monohydrochloride)	500	mg.
Vitamin A acetate	1,500	U.S.P. Units
Vitamin D	1000	U.S.P. Units
Thiamine mononitrate	0.75	mg.
Riboflavin	1.25	mg.
Niacinamide	7.5	mg.
Vitamin B_{12}	2.5	mcg.
Folic Acid	0.25	mg.
Ascorbic acid (from sodium ascorbate)	75	mg.
Pyridoxine hydrochloride	0.75	mg.
Calcium pantothenate	7.5	mg.
Iron ammonium citrate green (elemental iron 7.5 mg.)	50	mg.
Calcium gluconate (elemental calcium 139 mg.)	1.45	Gm.

Supplied: In 46 Gm. bottles with special Lactofort measuring spoon enclosed.

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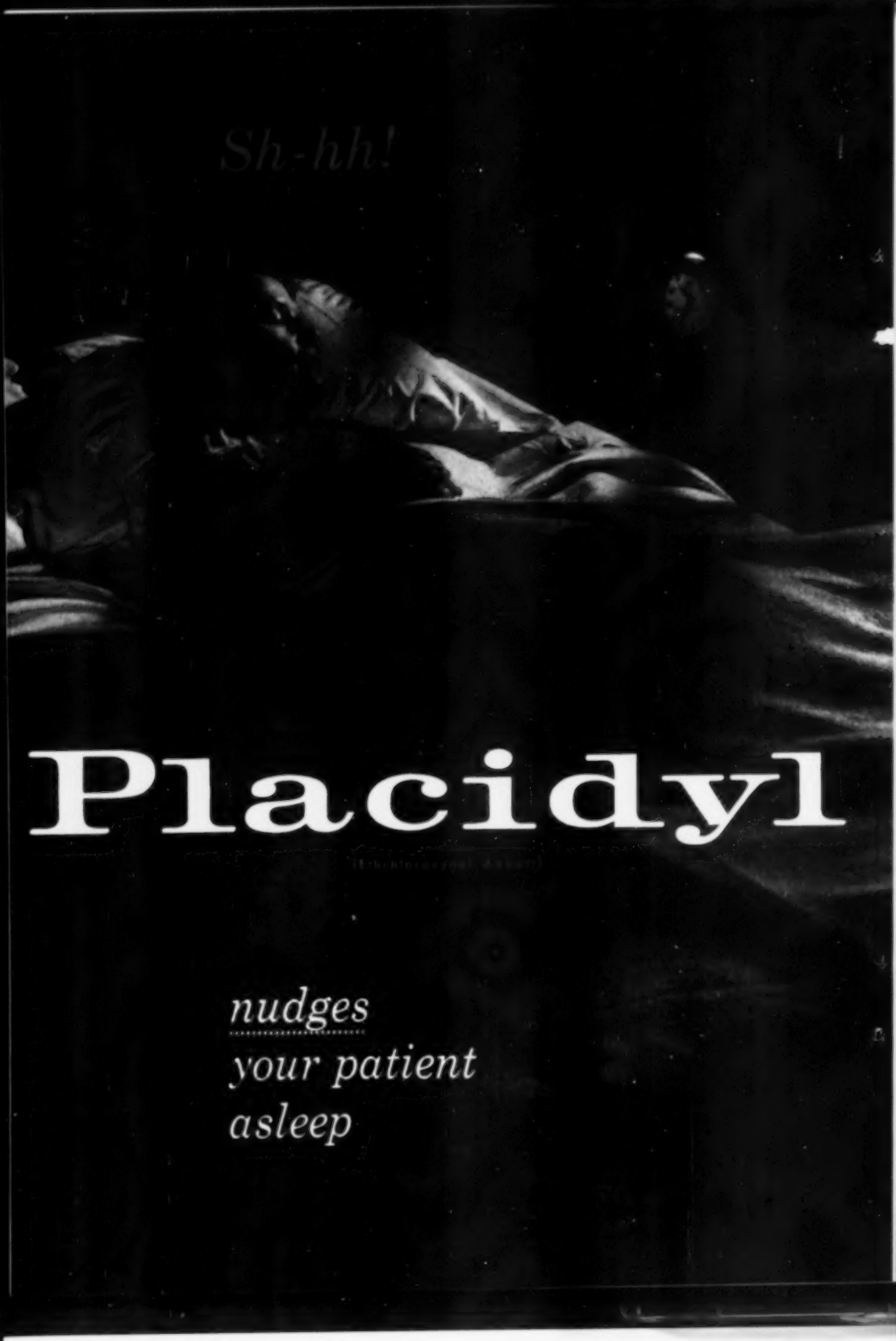
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Introducing Abbott's new non-barbiturate hypnotic

Placidyl offers a gentle new therapy for ordinary nervous insomnia.

It relaxes and calms the patient. Tranquil sleep comes within 15 to 30 minutes—should last all night.

Placidyl does not force patients into sleep; rather, it *induces* them to sleep naturally.

Hangover? Not a trace.

Even patients who take Placidyl after waking in the small hours rise clear-headed and refreshed.

Side actions? Virtually none. Not contraindicated in presence of liver or kidney disease. Doses to 1000 mg. show no effect on pulse, blood pressure, respiration, blood, or urine.

Profound hypnotic drugs remain justified for some insomnia patients. But for those whom you wish to give a safer, more gentle source of sleep . . . prescribe this mild new product. Abbott

Not related to the barbiturates, bromides, chloral hydrate, paraldehyde, etc. Available in 500 mg. capsules, bottles of 100. Adult dose for ordinary nervous insomnia 500 mg. at bedtime.

began to absorb some of the ideas. This soldier had very little political or socio-economic knowledge with which to resist brainwashing, compared with men who withstood brainwashing and its effects, partly because they already had well-formed hostility towards Communism.

On his return home, the soldier met with hostility from persons who attacked as traitors those who had been brainwashed. Many of his ideas were now in conflict with those accepted by American society. This led to confusion, anxiety, and eventually hospitalization.

The physicians suggested that treatment for this patient would include a kind of brainwashing in reverse, in which he would be rewarded and reinforced for behavior acceptable by his own society.

United States Becomes 'Medical Magnet'

The United States has become a "medical magnet" for physicians in Europe, Asia, Africa, and Latin America.

More than 5,000 foreign physicians came to this country during the year 1954-55 for study, according to a survey by the Institute of International Education and the American Medical Association.

They came from 83 different countries for internship and residency training at hospitals in 42 states, the District of Columbia, Hawaii, Puerto Rico, and the Canal Zone.

The survey of 1,177 hospitals, among those approved for internships and

residencies by the A.M.A. Council on Medical Education and Hospitals, indicated that there were at least 5,036 alien physicians in training. Not included in the study were immigrants and displaced persons.

Individual countries sending the most physicians were the Philippines, Canada, Mexico, Germany, and Turkey. Of the major geographical areas, the Middle, Near, and Far East had the largest representation.

Of the total, 620 or 12.3 per cent were women. In comparison, women made up only 5.2 to 5.7 per cent of American medical school graduating classes in the years 1952 through 1954. Over half of the women came from the Near, Far, and Middle East, with the Philippines sending the most.

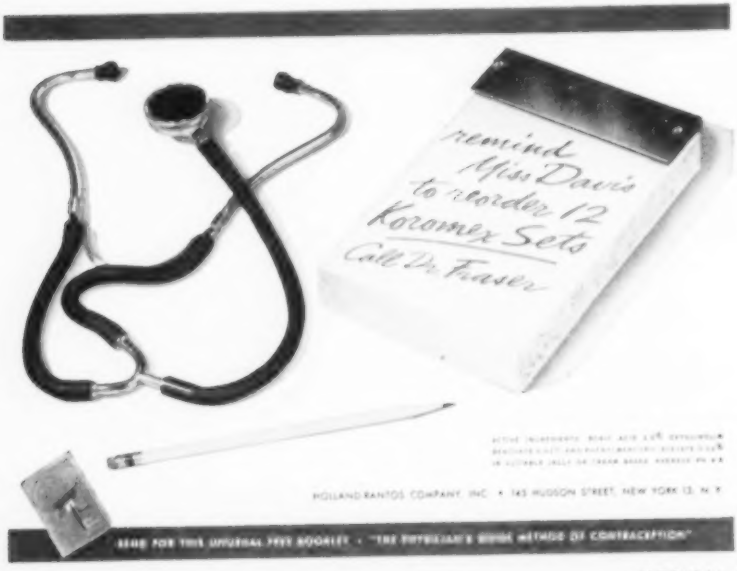
More than 2,000 of the physicians were in the United States on their own resources. Others were sponsored by at least 67 different agencies, including their own or the United States government, the United Nations, and religious, educational or philanthropic organizations. Many were sponsored by the hospitals in which they were training.

In addition to the large number of physicians in hospital internship-residency training, others visited this country as observers, professors, or guest participants in research. They represented 21.5 per cent of all foreign educators who visited the country during the year.

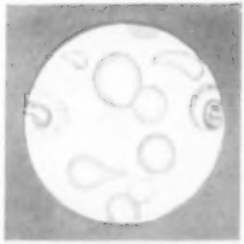
In comparison, only 3.6 per cent of all American educators visiting other parts of the world in 1954-55 were listed under medicine.

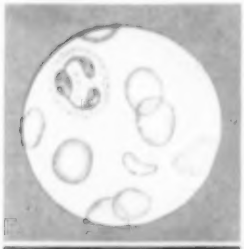
The survey was reported in a recent issue of the *Journal of the American Medical Association* by Dr. James E. McCormack, associate dean of gradu-

—Continued on page 150a



MORE THAN A HEMATINIC





HEPTUNA PLUS will correct most common anemias, of course.

But as you know, anemia is usually only one manifestation of a complex deficiency picture. [1-3]

So to HEPTUNA PLUS' potent hematopoietic factors, we've added vitamins A and D, the complete B complex, and 10 important minerals.

Is it a refractory anemia case? Try HEPTUNA PLUS.

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EACH SOFT, SOLUBLE CAPSULE CONTAINS:

Ferrous Sulfate, Dried, U.S.P.*	199 mg
Vitamin B$_{12}$, U.S.P.	5 mcg
Folic Acid, U.S.P.	0.33 mg
Ascorbic Acid, U.S.P.	50 mg
Cobalt (from Cobaltous Sulfate)	0.1 mg
Copper (from Cupric Sulfate)	1 mg
Molybdenum (from Sodium Molybdate)	0.2 mg
Calcium (from Dicalcium Phosphate)	37 mg
Iodine (from Potassium Iodide)	0.05 mg
Manganese (from Manganous Sulfate)	0.033 mg
Magnesium (from Magnesium Sulfate)	2 mg
Phosphorus (from Dicalcium Phosphate)	29 mg
Potassium (from Potassium Sulfate)	17 mg
Zinc (from Zinc Sulfate)	0.4 mg
Vitamin A (Fish Liver Oil)	5,000 U.S.P. Units
Vitamin D (Tuna Liver Oil)	500 U.S.P. Units
Thiamine Hydrochloride, U.S.P.	2 mg
Riboflavin, U.S.P.	2 mg
Pyridoxine Hydrochloride, U.S.P.	0.1 mg
Niacinamide, U.S.P.	10 mg
Calcium Pantothenate	0.33 mg
Desiccated Liver N.F. (undefatted)	150 mg

*Equivalent to 4.5 gr. Ferrous Sulfate U.S.P.

1. Cecil, R.L., and Loeb, R.F.: A Textbook of Medicine, W.B. Saunders Co., Philadelphia, 1951, p. 1012. 2. McLester, J.S.: Nutrition and Diet in Health and Disease, W.B. Saunders & Co., Philadelphia, 1949, p. 636. 3. Ibid., p. 627.

DOSAGE: one to four capsules daily, after meals.

SUPPLIED: bottles of 30 and 100 soft, soluble capsules.

CHICAGO 11, ILLINOIS

POERIG Rx

—Continued from page 49a

ate studies at Columbia University College of Physicians and Surgeons, and Arthur Feraru, head of the Central Index and Census Division, Institute of International Education, both of New York.

Arthritic Rehabilitation Program Outlined

The combined use of drugs and a physical rehabilitation program perhaps could "salvage from their invalidism" and return to "the dignity of living" many persons with active cases of chronic rheumatoid arthritis.

Results of such a program used for 38 patients at Goldwater Memorial Hospital, New York, were encouraging, according to Drs. Edward W. Lowman, Philip R. Lee, and Howard A. Rusk. They outlined the program in a recent issue of the *Journal of the American Medical Association*.

In the past rehabilitation of persons with active cases was restricted because of the danger of accelerating the disease process. Now cortisone and other drugs usually can control the spread of the disease, although they do sometimes produce undesirable side effects.

After the disease process is controlled, the program to reteach "activities of daily living" is begun. The patient is taught to perform such activities as eating and dressing without help and with maximum efficiency. As he succeeds in performing one act

—Continued on page 52a

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patients

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ABDEC DROPS give your youngest patients dependable multivitamin support, so important to optimal growth and development. A stable, nonalcoholic formulation—concentrated for easy administration—ABDEC DROPS mix readily with food, fluid, or formula, or may be placed directly on the tongue. There is no need for refrigeration. Supplied in 15 and 50 cc. bottles with graduated dropper.

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When
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bulk producers
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The Hydrophilic Colloid *So Palatable* That It *Insures* Patient Acceptance.

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L.A. Formula contains 50% Plantago ovata concentrate dispersed in lactose and dextrose. Available in 7 and 14 ounce cans.

Unsurpassed for the control of chronic constipation; valuable in the management of the simple diarrheas and obesity.

Write for samples

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WASHINGTON 9, D. C.

—Continued from page 152

he moves to another, always aiming at the highest efficiency within the limitations set by his crippled muscles and joints.

In some cases use of special mechanical devices, such as wheelchairs, crutches, or long-handled combs and forks, is taught.

The psychological outlook of the patient is "a major force" in determining his success, the doctors said. Feelings of hopelessness, frustration, and dependence often develop because of the length and pain of the disease. Psychologists help the patient in overcoming such feelings and in setting practical goals of achievement.

As the patient prepares to return home, social workers assist him in making any necessary adjustments, such as moving to a more conveniently arranged home. Job placement offers the most difficulties, because arthritics require relatively sedentary jobs, which are limited. Retraining, following vocational testing, is sometimes part of the rehabilitation.

In the Goldwater experiment, all 38 patients showed some improvement. Of the 18 patients who were severely disabled, 14 have been discharged from the hospital. Seven of these are totally self-sufficient and one is employed. Average disability in this group dropped from 60 to 29 per cent after two years of treatment.

All 20 of the less severely disabled patients have been discharged from the hospital. Fifteen are totally self-sufficient and seven of these have jobs.

—Continued on page 154

specific

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in diaper dermatoses

Diaparene® CHLORIDE

FITS YOUR TREATMENT TO THE CAUSE

FECAL IRRITATION

Diaparene PERI-ANAL

FOR: Peri-Anal Dermatitis

CRITERIA: Inflammation centered around the anus from 3 to 4 cms. in diameter and frequent stools.

CAUSE: Transitional stools in the newborn, diarrhea or following oral antibiotics.[1]

MODE OF ACTION: Provides a skin coating with a competitive protein substrate, plus anti-enzymatic and antibacterial action in a water-repellent, cod-liver-oil base.[2,3]

URINE IRRITATION

Diaparene OINTMENT

FOR: Ammonia Dermatitis

CRITERIA: Presence of ammonia odor and buttock-inflammation in apposition to wet diaper.

CAUSE: Free ammonia liberated by urea-splitting organisms.

MODE OF ACTION: Prevents ammonia formation in voided urine with an antibacterial in a water-miscible base[4,5] . . . adjuvant therapy to routine Diaparene Rinse impregnation of diapers.[7,6]

1. Markheim, S. D., et al: "Further Observations on Anorectal Complications Following Aureomycin, Terramycin and Chloromycetin Therapy." N. Y. State Jrnl. Med., 54:37-1, Jan., 1954.
2. Curry, J. C. and Barber, F. W.: Bacteriological Proceedings, 1951, of The Society of Am. Bact., page 23.
3. Grossman, L., St. Francis Hospital, Miami Beach, Fla., to be published.
4. Needelman, M. L., et al: Jrnl. Ped., 37:762, Nov., 1950.
5. Bleier, A. H., et al: Arch. Ped., 69:445, Nov., 1952.
6. Benson, R. A., et al: Jrnl. Ped., 31:369, Oct., 1947.
7. Ibid: Jrnl. Ped., 34:49, Jan., 1949.

PHARMACEUTICAL DIVISION, HOMEMAKERS' PRODUCTS CORPORATION, NEW YORK 10, N. Y. TORONTO 10, CANADA

—Continued from page 152a

Disability dropped from 30 to 4 per cent in this group.

While the program is long and expensive, it may well pay for itself in the long run either by returning the patient to work or by releasing for employment a person who has been caring for him, the authors said.

Physician Doubts Existence of "Ulcer Personality"

Doubt as to "the nature or even the existence of a specific ulcer personality" was expressed today by a Cleveland physician.

It has become common in the last few years for doctors and the public to refer to certain persons as being of the "ulcer type." Articles and even a book have been written on the subject.

Yet investigators cannot agree on what goes to make up the "peptic ulcer personality," Dr. Harold P. Roth said in a recent issue of *Archives of Internal Medicine*.

He found that a number of different personalities were described as typical in various studies on the topic. "There was no whole personality or feature of personality that was agreed upon by as many as a third of the investigators," he said.

Personality traits most frequently mentioned were drive, conscientiousness, and anxiety. "Although other traits were described, the statements about most of them were contradic-

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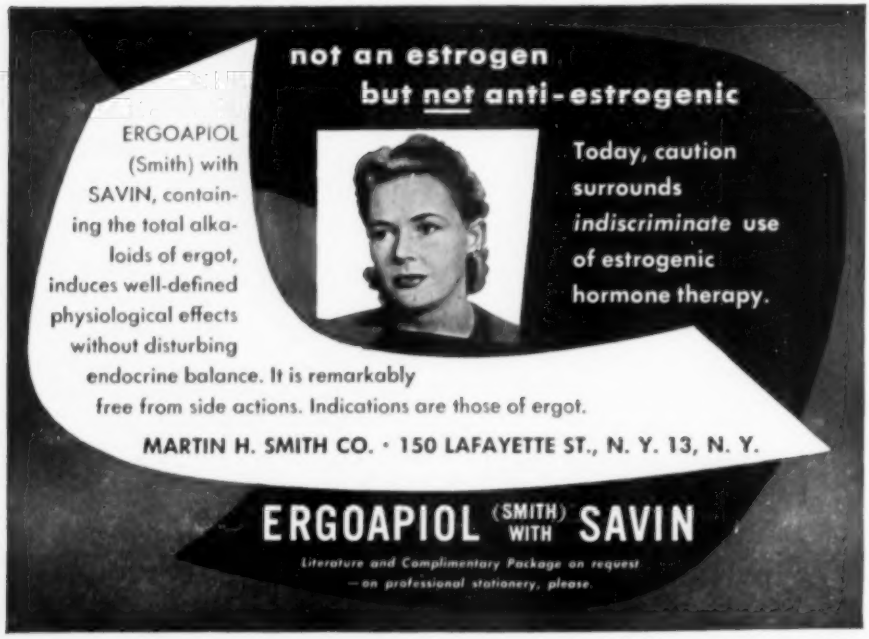

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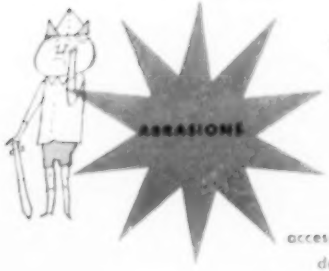

- Xylocaine Ointment provides unusually rapid, and deeply penetrating anesthesia without the drawback of toxicity, sensitization or irritation. Xylocaine is unique in this respect.
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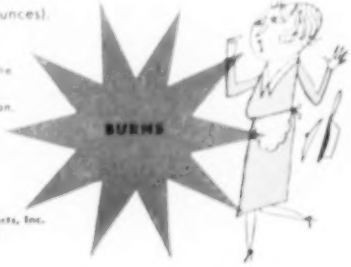
- Available in a water soluble, nonstaining vehicle as 2.5% and 5% Xylocaine base in collapsible tubes or wide mouth jars, each containing 35 grams (approx. 1.25 ounces).

Xylocaine Ointment is now made available at the request of many physicians, surgeons, and anesthetists who routinely use Xylocaine Solution.



ASTRA

Astra Pharmaceutical Products, Inc.
Worcester 6, Massachusetts

*U. S. Patent No. 2,441,498

—Continued from page 154a

tory," he said.

Some authors suggested that ulcer patients had a specific type of conflict. But they did not always agree on the nature of the conflict nor whether the conflict was associated with a specific personality type.

The conflict most frequently reported was between feelings of passivity and feelings of activity and independence. Because this same conflict is seen in persons without ulcers, "we must know how often this conflict can be found in the general population before we can decide how significant is the fact that it is found in ulcer patients," Dr. Roth said.

"We cannot say whether the fact that a number of investigators described the same personality features is significant, for this may be due to a defect in their technique," he said.

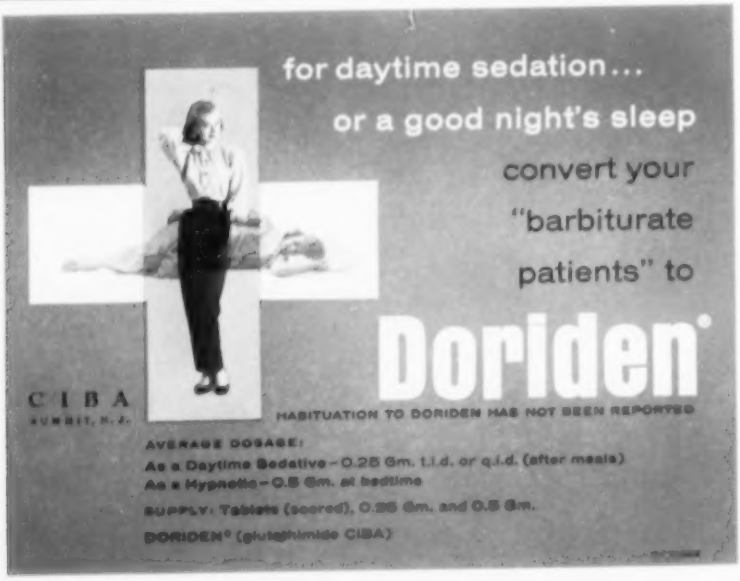
In half of the studies no method of study was outlined. Some were based on interviews, psychoanalysis, and psychological testing.

No distinction was made between patients with gastric ulcer and those with duodenal ulcer nor between male and female patients in many of the studies. Yet investigators who studied these groups separately found there differences in personality.

"Conclusions about the ulcer personality in the general population have been drawn from studies of samples that were not representative," Dr. Roth said.

"Usually the author did not report how often he found a given characteristic, such as ambition, in his patients.

—Continued on page 158a



She'll enjoy this pregnancy

Fifty per cent of all pregnant women – even those on a "good" prenatal diet – suffer calcium deficiency symptoms.*

the wrong calcium worse than none

New evidence further shows that because of calcium-protein antagonism, time-honored calcium phosphate supplements may actually cause a deficiency, just when optimum levels are desired. And high-protein diets are also rich in calcium-draining phosphorus. Thus leg cramps are a minor symptom of major significance: their presence may indicate seriously low calcium levels.

reduce phosphate ... increase calcium

Calcisalin, a complete prenatal supplement, containing 100% of the MDR for vitamins and iron, is also completely physiologic. Phosphate-free and phosphorus-eliminating, it helps prevent hypocalcemia at both points of origin: • calcium lactate assures readily assimilable calcium, free from the depressing action of phosphorus • aluminum hydroxide gel takes up excess dietary phosphorus without interfering with the value of other nutrients.

Note: "Noncomplainers": many patients consider leg cramps "normal" and complain only when cramps are severe. Thus the number of complaints does not truly reflect the higher incidence of calcium depletion. To safeguard against serious, "silent" calcium depletion, all women who enjoy a high-protein prenatal diet can benefit from Calcisalin's phosphate-free, phosphorus-eliminating properties.

Dosage: Two tablets three times daily.

Available: Bottles of 100 tablets and in 8-ounce nursing bottles containing 300 tablets.

*Wolff, J. R.: [illegible] M. J. [illegible] 1954.

Calcisalin®

WARNER-CHILCOTT

—Continued from page 156a

. . . Generally he reported his conclusions, not his data," he said.

"An entirely satisfactory" method for evaluating personality has not been developed, nor has a method for comparing ulcer patients with ulcer-free persons, Dr. Roth said.

Genetics Offers Means of Changing Man

Man has within his grasp more power to change future generations through breeding than he has wisdom to direct changes for the best results.

An editorial in a recent issue of the *Journal of the American Medical Association* said genetics, the science of heredity, offers the possibility of changing the race. However, no means for improvement of human stock has yet been devised.

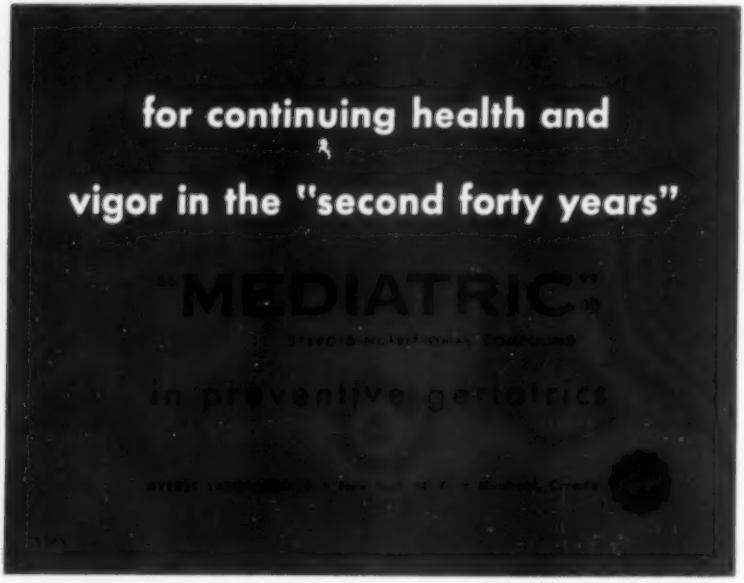
There are many difficulties, resulting largely from the complicated behavior of genes, the biological factors which determine heredity.

For instance, it may be possible to control one gene, but it is hard to tell how it will be influenced by other genes. In other words, the effect of a gene may depend on "the company it keeps."

Another problem is the inability to predict long-term results of manipulating genes.

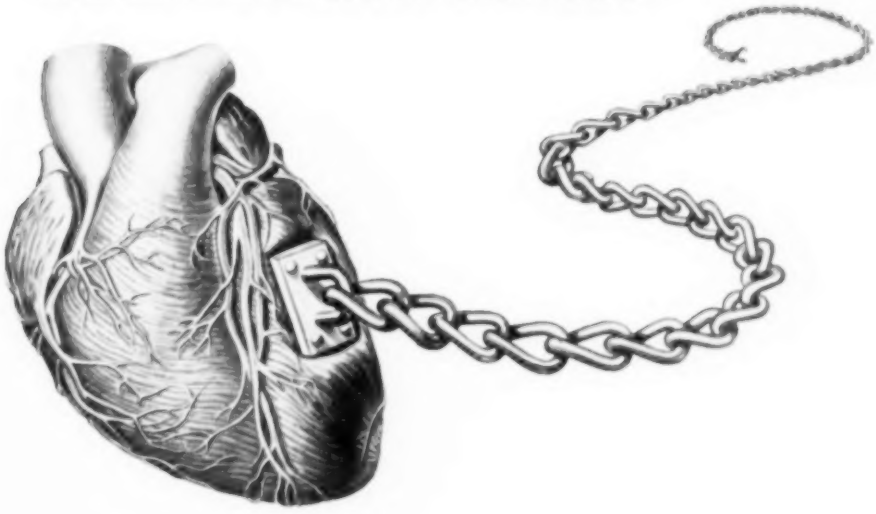
"Selective breeding," as used in cattle, has been suggested as a method of improvement, but this is not likely to gain wide acceptance because of the "violent emotional reactions such pro-

—Continued on page 166a



in your anginal patient...

break the chain of "heart-consciousness"



Your anginal patient can be freed from his "heart-consciousness" for a wider range of activities by the daily administration of Nitralox which aids in protecting him against the bodily and emotional factors which so often precipitate anginal seizures. Nitralox generally lessens the frequency and severity of attacks, will often lower nitroglycerin requirements, increase exercise tolerance and improve the electrocardiogram.

In anginal patients with hypertension and tachycardia, Nitralox has the added advantage of reducing the blood pressure and slowing the pulse. It has no such effects in normotensives with normal heart rates.

Nitralox combines a coronary vasodilator with prolonged action (10 mg. pentaerythritol tetranitrate – PETN) with a nonbarbiturate tranquillizing and bradycrotic agent (1 mg. purified mixed Rauwolfia alkaloids – the alseroxylon fraction) and is intended for long-term prophylactic therapy. While some patients experience beneficial effects within 24-48 hours, it takes about two weeks before Nitralox produces its full effect from the recommended dosage of 1-2 tablets q.i.d. before meals, and at bedtime.

NITRALOX

for long-range management of anginal attacks

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for your dyspeptic, geriatric, underweight, and gallbladder patients

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digestant tablets

for improved nutritional status... clinical response

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Each CONVERTIN Tablet provides:
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Betaine Hydrochloride . . . . . 130.0 mg.
(Provides 5 minims Diluted Hydrochloric Acid U.S.P.)
Oleoresin Ginger . . . . . 1.600 gr.
Surrounding an enteric coated core of:
Pancreatin (5 x U.S.P.) . . . . . 62.5 mg.
(Lipase 250 mg.)
Desoxycholic Acid . . . . . 50.0 mg.

DOSAGE: Two tablets with or just after meals. Dose may be reduced at discretion of physician, usually after first week.

SUPPLIED: In bottles of 84 and 500 tablets.

Available on prescription only.

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Ethical Medicinals
KANSAS CITY, MISSOURI

posals automatically arouse."

"The widespread use of a 'perfect donor' through artificial insemination might lead to too great a uniformity in a world where diversity is still highly desirable," the editorial said.

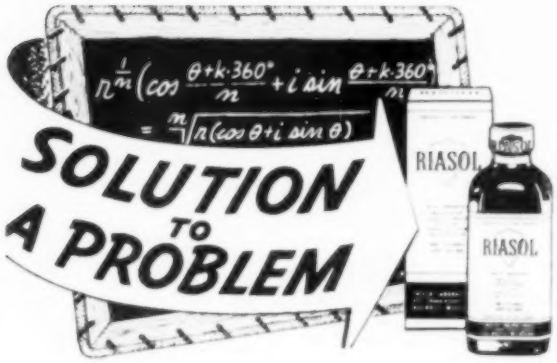
In addition, such a donor might spread hidden bad traits through a large segment of the population before they could be detected. Inbreeding, as has been shown in the past by various royal families, brings hidden traits into the open. "If these are harmful, as they are more often than not, inbreeding will increase the number of persons afflicted," the editorial said.

The proportion of persons with mental and physical defects is increasing in modern civilization because advances in medical science make it possible for them to live longer, the editorial said.

None of the measures advocated to prevent degradation of human stock, such as sterilizing mental defectives, have "made more than a feeble impression on the problem as a whole."

While physical traits are more nearly determined by heredity, they are less influenced by environment than are mental traits. "Social traits or personality, although affected by heredity, are altered by environment with the greatest ease."

The editorial concluded, ". . . it is easier to define good environment than good heredity. So far, the power to change man genetically exceeds the wisdom needed to know in what direction genetic controls should be applied to achieve the best results."



Albert Einstein's (1879-1955) fundamental theory of relativity has taught us to judge results by comparison. To determine the true value of a drug, investigators compare it with a control series.

A clinical study[1] of RIASOL showed definite improvement in 76% of a series of resistant psoriatics. In another series[2] treated with various other medications, remissions occurred in only 16½% of the cases.

Thus by simple arithmetic RIASOL proved to be 461% as effective as other medications generally in the treatment of psoriasis. Relativity proves the true value of RIASOL by comparison with other therapies.

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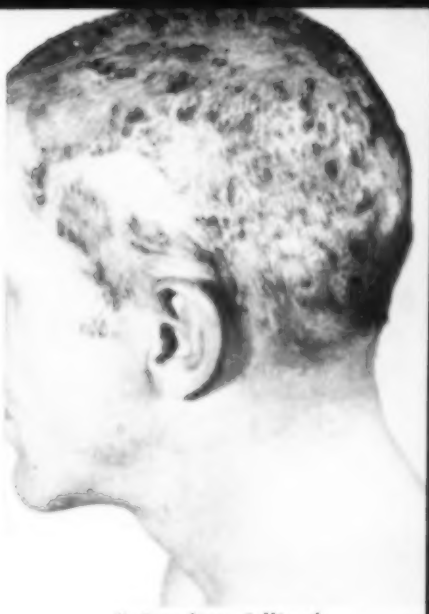
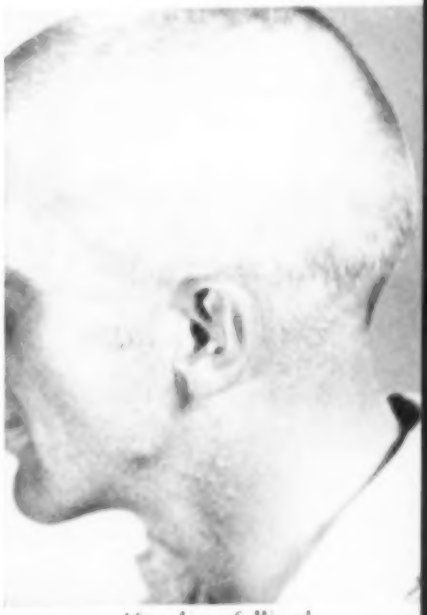
Apply daily after a mild soap bath and thorough drying. A thin, invisible, economical film suffices. No bandages required. After one week, adjust to patient's progress.

RIASOL is supplied in 4 and 8 fld. oz. bottles at pharmacies or direct.

1. *M. Rec.* 151:397, 1940.
2. *Arch. Dermat. & Syph.* 35:1051, 1937.



Before Use of Riasol



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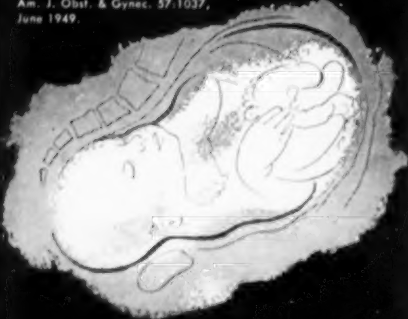
Am. J. Obst. & Gynec. 57:1037, June 1949.



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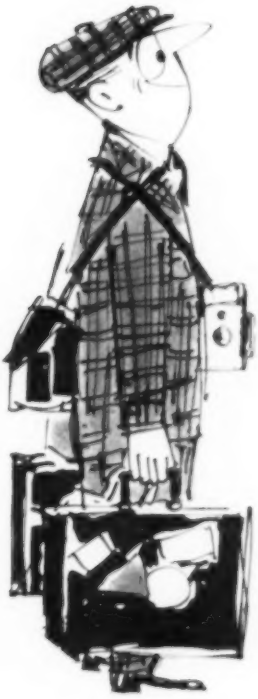

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MEDICAL TIMES, SEPTEMBER, 1955

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REFERENCES: 1. Am. Heart J. 18:425, 1939.

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